University of Alberta

Polymerization and Use of Rhodium and Ruthenium Catalysts for the Cycloisomerzation Alder-Ene Reaction

by

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Abstract

A derivative of 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (BINAP), (*R*)-5,5'-norimido-BINAP (N-BINAP) was synthesized and complexed with rhodium and ruthenium. These complexes were subsequently used in the cycloisomerization Alder-ene reaction. [Ru((*R*)-BINAP)(η^5-C_8H_{11})]BF_4, [Ru(MeCN)((*R*)-BINAP)(COD)]BF_4, [Ru(MeCN)((*R,R*)-Norphos)(COD)]BF_4, [Rh(N-BINAP)NBD]BF_4 and [Rh(N-BINAP)NBD]BF_4 were tested for homogeneous activity towards the cycloisomerization reaction. No activity was detected for the ruthenium complexes, though the rhodium pre-catalysts took the reaction to completion. The rhodium complexes were both successfully polymerized and deposited on a solid support. No product was detected when used in the cycloisomerization reaction.

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List of Abbreviations

AcOH	Acetic Acid
AIBN	Azobisisobutyronitrile
BINAP	(*R*)-2,2'-bis(diphenylphosphino)-1,1'-binaphthyl
CM	Cross metathesis
COE	Cyclooctene
Cy	Cyclohexyl
dba	Dibenzylideneacetone
DCE	1,2-Dichloroethane
DMF	Dimethylformamide
DMG	N,N-Dimethylglycine
dpen	1,2-Diphenylethylenediamine
EGDMA	Ethylene glycol dimethacrylate
ee	Enantioselective excess
EMA	Ethyl methacrylate
MeCN	Acetonitrile
NBD	Norbornadiene
N-BINAP	(*R*)-5,5'-norimido-BINAP
NHC	1,2-bis(2,4,6-trimethylphenyl)-4,5-dihydroimidazol-2-ylidene
NMR	Nuclear magnetic resonance
Norphos	2,3-bis(diphenylphosphino)-bicyclo[2.2.1]hept-5-ene
PdAS-V	Poly{dichlorobis[(N-isopropylacrylamide)5-co-(4-diphenylstyryl-phosphine] palladium
Py	Pyridine
RCM	Ring closing metathesis
ROMP	Ring opening metathesis polymerization
THF	Tetrahydrofuran
TOF	Turnover frequency
TON	Turnover number
xylyl-BINAP	(*R*)-2,2'-bis(di(3,5-xylyl)phosphino)-1,1'-binaphthyl

Chapter 1: Introduction

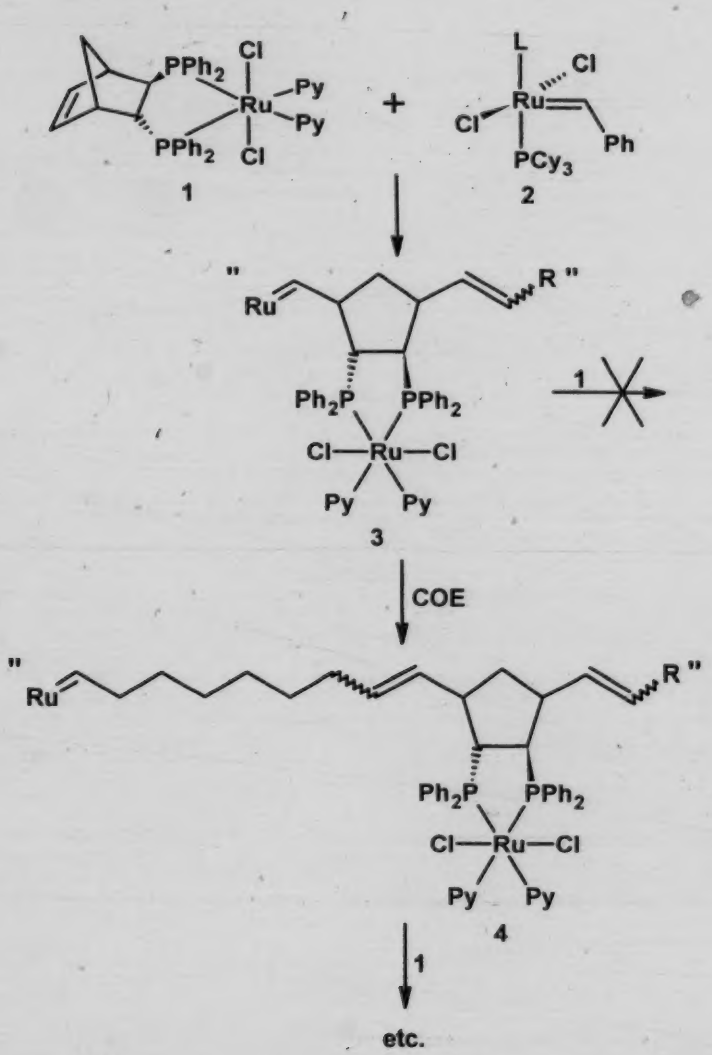
Asymmetric catalysis has become one of the most important fields in chemistry.[1-5] The pharmaceutical, agrochemical, flavouring, fragrance and vitamin industries spend billions of dollars every year on research and development of asymmetric synthesis. Biologically active molecules are often chiral with only one enantiomer having the properties of interest. The opposite enantiomer can be harmful, have no effect, or can diminish the activity of the desired enantiomer. Thus, mixtures of enantiomers must often be resolved to obtain the desired enantiomer in homochiral form. Such resolutions carried out on an industrial scale are often difficult and costly. Asymmetric catalysis using trace amounts of homochiral catalyst is the most efficient synthetic method to produce chiral products in near homochiral form. Having pure homochiral products prevents the need for separation of the desired enantiomer from a mixture of products. Further, often the chiral molecules produced by asymmetric catalysis are difficult or impossible to obtain using classical, non-catalyzed means. Unfortunately, the catalysts used in asymmetric catalysis usually contain an expensive, toxic heavy metal in the active site. These catalysts typically last for only one reaction as they are often reactive, air sensitive, and difficult to isolate after use without destroying their activity. As well, the removal of all traces of the toxic heavy metal from the product of a catalytic reaction is difficult, expensive, and it can lead to residual metal catalyst being present in the product or environment if done improperly.

A solution to these problems is to synthesize a reusable, heterogeneous, asymmetric catalyst which can be easily removed from the reaction mixture. Polymerization of a homogeneous catalyst has been a pursued method to create a

heterogeneous catalyst which can be filtered from the reaction mixture. Polymeric catalysts are usually made using radical polymerization of vinyl derivatives of arenes and phosphines,[6, 7] condensation reactions between acid derivatives and amines or alcohols,[8-10] condensation polymerizations between diamines and diisocyanates,[9] or Suzuki-type couplings.[11] The presence of a metal centre can interfere with each of these reactions and so they are often carried out by polymerizing the chiral ligand first, and then metallating the resulting polymer. Another approach using the reactions listed above is to graft the ligand to a polymer support prior to metallation. Limited mass transport of metal through the polymer often results in incomplete metal binding to the ligand sites during these procedures.

The Bergens group has reported one of the few examples using a metal-phosphine complex as a monomer for polymerization. A methodology was developed that uses ring opening metathesis polymerization (ROMP) with a metal-phosphine monomer to form a metal catalyst-containing polymer.[12, 13] The Norphos ligand (Norphos = 2,3-bis(diphenylphosphino)bicyclo[2.2.1]hept-5-ene) was complexed to a metal and this was polymerized with First Generation Grubbs' catalyst and a spacing monomer, cyclooctene (COE), to create a metal catalyst co-polymer. Equation 1 shows the ruthenium catalyst co-polymer produced by former Bergens graduate student Okwado Akotsi.

Akotsi's attempts to polymerize the Ru complex directly were unsuccessful after 24 h due to steric crowding. COE was therefore employed as a spacing monomer, or co-monomer, as it is less crowded than the Ru complex **1**. The strained double bond in the Norphos ligand, however, is intrinsically more reactive towards ROMP than the double bond in COE. An initial reaction between **1** and Grubbs' catalyst **2** results in an



Equation 2. Ruthenium catalyst co-polymer synthesized by Ralph et al for the hydrogenation of acetonaphthone.[13] Compound **2** is Grubbs' Catalyst L = PCy_3 (Cy = cyclohexyl) in First Generation Grubbs' Catalyst or L = NHC (NHC = 1,3-bis(2,4,6-trimethylphenyl)-4,5-dihydroimidazol-2-ylidene) in Second Generation Grubbs' Catalyst.

alkylidene species such as **3**. Reaction of **3** with another molecule of **1** can not happen due to the bulk of the two groups. **3** can react with COE, however, to generate **4,** removing the steric effects generated by neighbouring ruthenium complexes and allowing the polymerization to proceed. An increase in rate of polymerization was found when the ratio of COE:**1** was increased. A ratio of 4:1 resulted in the polymerization rate

increasing 12 times over the 1:1 ratio. The ratio of COE:**1** can also affect the swellibility of the polymer and accessibility to the metal. By increasing the ratio, a polymer will form that is more easily swelled by solvents.

The polymerized ruthenium catalyst shown in Equation 1 was converted into the 1,2-Diphenylethylenediamine (dpen) compound and then successfully reused 10 times for hydrogenation of *1'*-acetonaphthone with 85% *ee*. This was the highest number of reuses of an insoluble polymer-based hydrogenation catalyst without loss in *ee* or rate that does not require a swelling solvent prior to the formation of the group's next catalytic cycle.[12, 13]

With the ROMP methodology outlined above in mind, Ralph recently synthesized a *5,5'*-BINAP derivative, *(R)-5,5'*-dinorimido BINAP (N-BINAP), shown in Figure 1. BINAP was chosen as the preligand as it is the most widely used and versatile ligand in enantioselective catalysis,[14] and it gives higher selectivity than the Norphos catalyst used in their previous work.[13]

This BINAP derivative has two norbornyl groups at the *5* and *5'* positions in the backbone providing a ROMP-ready strained double bond for polymerization without interfering with the chiral environment of the active site. A BINAP-based ligand which was derivatized on both sides was sought in order to obtain an extended, 3-dimensional catalyst-organic framework with the catalyst complex as cross-linking units. Figure 2 shows a schematic of the 3D matrix obtained by the ruthenium-phosphine complex synthesized by Ralph et al. This results in a minimization of catalyst leaching and the cross-linking adds rigidity to the framework of the polymer catalyst.

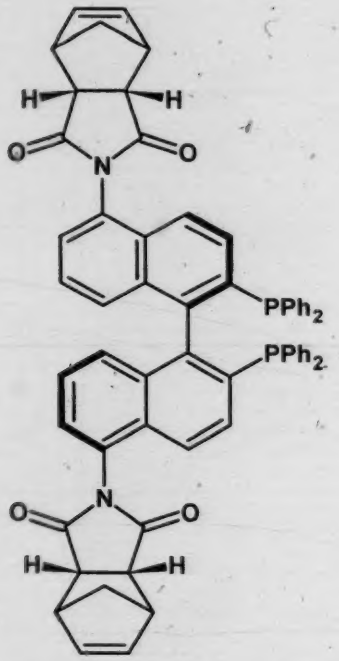


Figure 1. (*R*)-*5,5'*-dinorimido BINAP synthesized by former Bergens graduate student Corbin Ralph.[13]

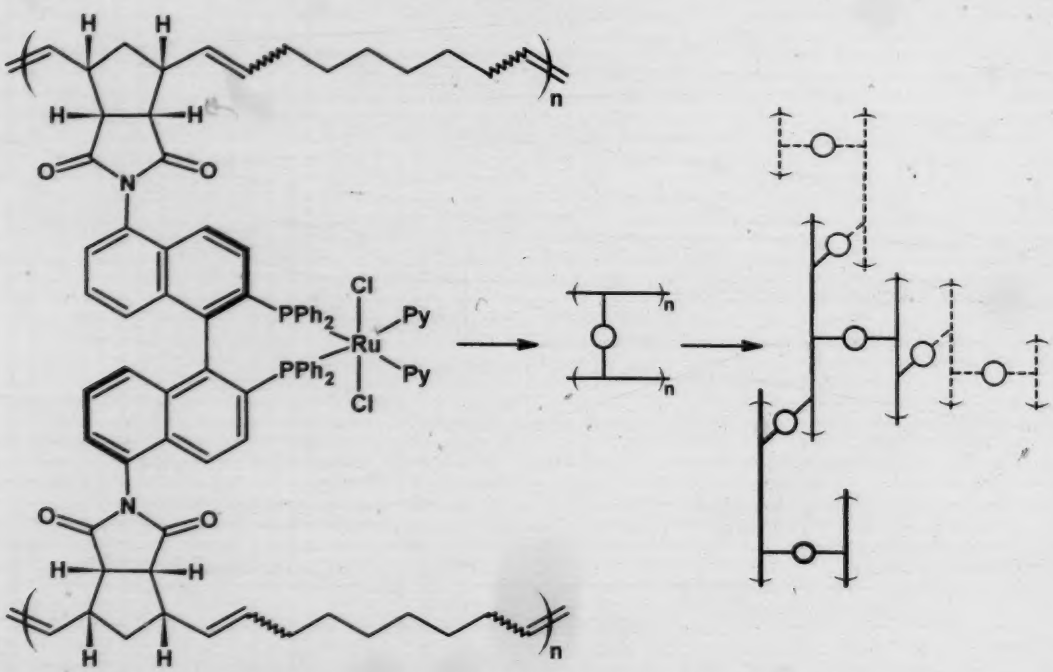
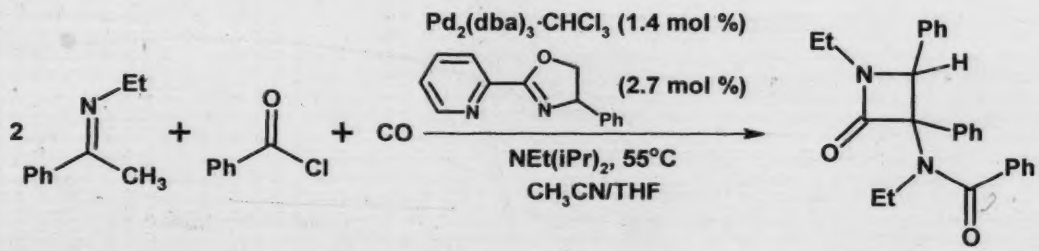


Figure 2. Schematic representation of the extended 3D framework containing by the Ru-based hydrogenation catalyst synthesized by Corbin Ralph.[13]

The ruthenium-catalyst containing polymer shown in Figure 2 was prepared and used successfully in catalytic asymmetric hydrogenations. This catalyst was reused 25 times in the hydrogenation of *1'*-acetonaphthone at 0.1% catalyst loading without loss in activity or enantioselectivity and without detectable Ru leaching.[13] This system has provided more reuses than any previous heterogenized hydrogenation catalyst.

The success of Ralph and Bergens' methodology and ligand led us to search for a carbon-carbon bond forming reaction to extend the application of their achievements beyond hydrogenation reactions. Catalytic C-C bond formation has become a fundamental tool of organic synthesis. Without it, starting materials would have to be more complex, thereby making the synthesis of natural products and their derivatives difficult and expensive. The controlled formation of carbon-carbon bonds gives a diversity of products from relatively simple starting materials. For example, Arndtsen et al. use a one-pot synthesis to form β-lactams from simple imines, acid chlorides and carbon monoxide using a palladium catalyst.[15] Equation 2 shows one of the reactions carried out. β-Lactams are the basic building blocks of biologically relevant molecules such as penicillin, nocaricins and cephalosporins.



Equation 2. One of Arndtsen's palladium-catalyzed β-lactam synthesis from imines, acid chloride and carbon monoxide.[15] dba = dibenzylideneacetone

Much has been done to prepare polymer supported catalysts for C-C bond formation since the mid-90's. Numerous reactions have been catalyzed and include oligomerizations, isomerizations, Heck reactions, Suzuki couplings, olefin metathesis reactions, hydroformylation, Pauson-Khand reactions, and cyclopropanations.[16-24] Three of the more prominent reactions are olefin metathesis, Heck reactions, and Suzuki couplings, and will be expanded upon herein.

Olefin metathesis has come into widespread use since the synthesis of the ruthenium based-catalysts of Grubbs and Fu and the molybdenum-based catalysts of Schrock and Hoveyda.[25] The available ruthenium catalysts have the advantage of being more air and water stable than the molybdenum counterparts, but both sets of catalysts are functional group tolerant and capable of high activity. With the increased use of olefin metathesis reactions in organic synthesis, polymer supported metathesis catalysts are becoming prominent. [18, 21, 26-42] Figure 3 shows the closely related variety of reactions which can be performed through olefin metathesis including (a) ROMP, (b) ring closing metathesis (RCM) and (c) cross metathesis (CM).[32] This variation is part of what makes this group of reactions so useful in organic synthesis.

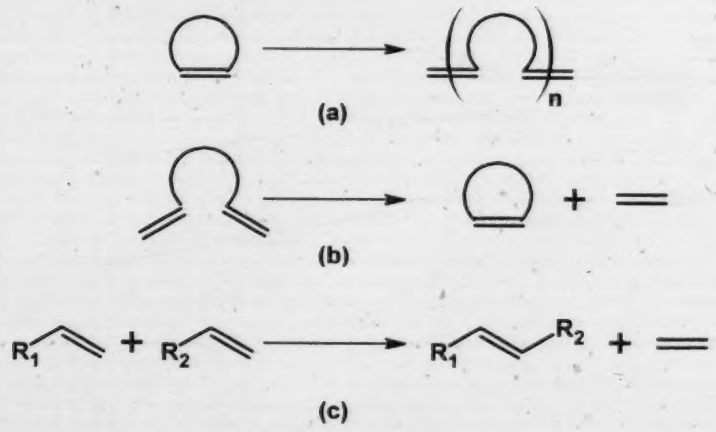


Figure 3. Olefin metathesis reactions which can take place. (a) ROMP, (b) RCM and (c) CM.

One of the first reusable metathesis catalysts was synthesized by Barrett and Braddock. Vinyl polystyrene was used to support their ruthenium-based metathesis catalyst, shown in Figure 4.[43-45]

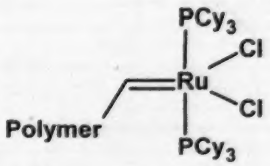
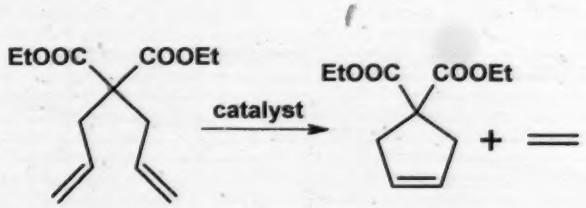


Figure 4. Barrett and Braddock's 'boomerang' olefin metathesis catalyst supported by a poly(vinyl polystyrene) backbone.[43-45]

This catalyst, synthesized by mixing Grubbs' catalyst with vinyl polystyrene, is termed a 'boomerang' catalyst because the catalyst is released from the polymer to perform the reaction and returns to the support upon completion. It was found to have comparable activity in RCM reactions to its homogeneous analog in seven separate types of RCM reactions. This catalyst has been reused up to three times in the RCM of diethyl diallylmalonate, shown in Equation 3, and the methodology derived by this work has been successfully adapted by other groups as well.[18]



Equation 3. The RCM of diethyl diallylmalonate carried out by Barrett and Braddock.[18]

Non-porous supports, or monoliths, made from ROMP reactions have allowed for continuous flow through reactors to be designed. These types of reactors avoid the need to filter off supported catalyst which eliminates time between runs as substrate can pass

over the catalyst continuously and catalyst-free product can be collected at the bottom. Other problems, such as those associated with stirring and splashing of the reaction mixture, are also alleviated by the flow through system. The 'boomerang' type of reusable catalyst, however, is unsuitable for flow systems as catalyst is eluted. A higher metal contamination of the product is also present as deteriorated catalyst is unable to reattach to the solid support. A stronger, more permanent backbone-catalyst bond allows the metal to stay bound to the support and perform the reaction without catalyst leaching into solution.

Buchmeiser et al. have grafted a ruthenium-based catalyst onto a ROMP-synthesized monolithic support.[26] This catalyst has been used for RCM in a flow through reactor. Batch reactions, which consists of the supported catalyst being placed in the substrate mixtures and stirred to carry out the desired reactions and the resulting mixtures filtered to remove the catalyst, were also carried out for comparison. The batch reaction resulted in turnover numbers (TONs) of 250 in the RCM reaction of diethyl diallylmalonate while TONs of up to 500 were obtained in the flow through reaction system. Figure 5 shows the structure of the monolith-supported catalyst.

Another method of polymerized catalyst generation was used by Hoveyda and Shrock when they developed the first reusable polymer supported chiral catalyst for enantioselective olefin metathesis.[46] This catalyst, shown in Figure 6, was prepared by first polymerizing the dialcohol ligand using radical co-polymerization with styrene followed by metallation of the polymer with the molybdenum complex.

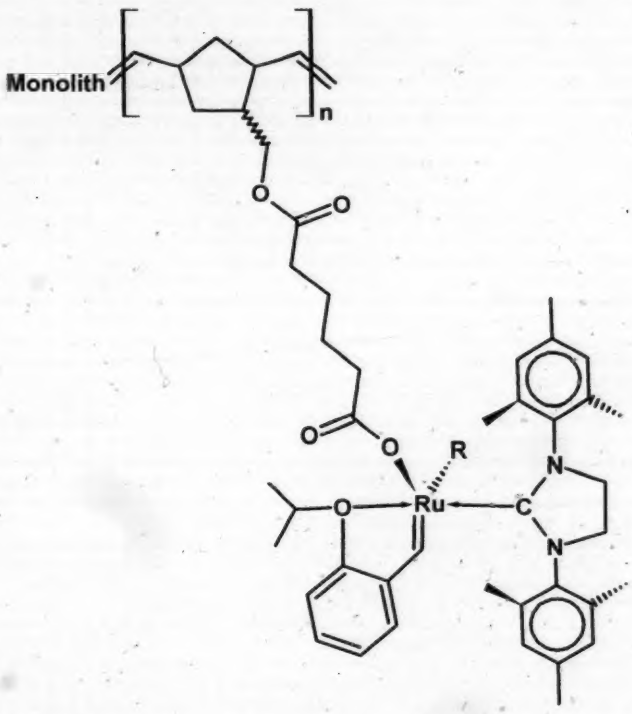


Figure 5. The monolith-supported metathesis catalyst used in batch and flow through column reactions by Buchmeiser et al.[26]

This supported catalyst has shown lower activity towards asymmetric ROM and RCM reactions than the homogeneous catalyst, though similar or higher enantioselectivity was achieved. A number of reactions were tested, one of which is shown in Equation 4. Upon filtration, the catalyst was reused up to three times with little loss in selectivity, though the activity decreased and a longer reaction time was needed for high yields due to metal leaching.

The Heck reaction is another important and versatile method of C-C bond formation. Generally, an olefin reacts with a halide or triflate in the presence of a palladium catalyst and base to form the new bond, as shown in Equation 5.

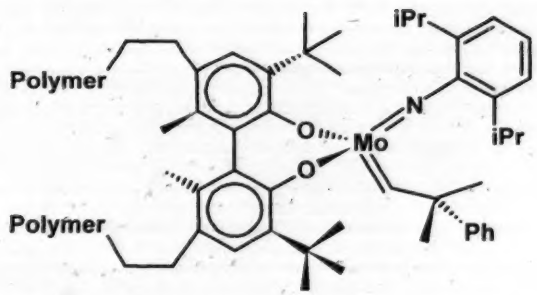
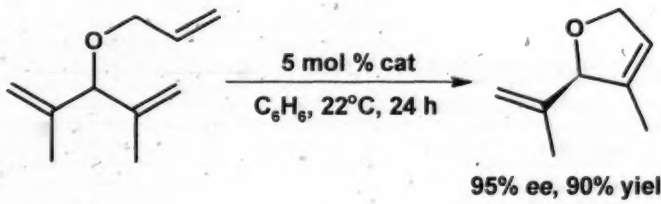
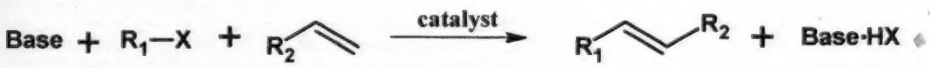


Figure 6. Reusable enantioselective olefin metathesis catalyst synthesized by Hoveyda and Schrock. The polymer is a styrene poly(vinyl alcohol) formed through radical polymerization initiated by benzoyl peroxide.[46]



Equation 4. RCM reaction carried out by Hoveyda and Schrock using the supported metathesis catalyst shown in Figure 6.[46]

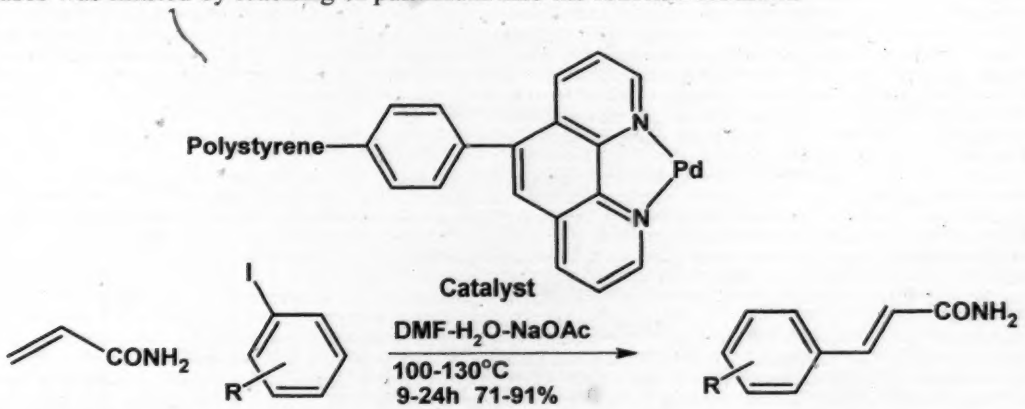


Equation 5. Heck reaction. X = halide, triflate. A palladium-based catalyst is the most widely used.

Heck reactions are used in the formation of pharmaceuticals, antioxidants, ultraviolet absorbers and fine chemicals.[47] Examples of these molecules include *p*-methoxycinnamic acid 2-ethyl hexyl ester (UV absorber and antioxidant), taxol (anticancer drug), and 6-methoxy-2-vinylnaphthalene (fine chemical used as a pharmaceutical intermediate).

Zhang et al. have used a [poly(styryl)phenanthroline] palladium polymer as a heterogeneous catalyst for Heck arylation, an example of which is shown in Equation 6.[47]

Different bases were tested in the coupling of acrylamide with iodobenzenes. It was found that the lifetime of the catalyst was dependant upon the base used. The catalyst was recovered and reused up to 10 times when Bu_3N (the base typically used in Heck reactions) was replaced with a dimethylformamide (DMF)-H_2O-NaOAc mixture. This catalyst was reused more than any previous polymerized Heck catalyst, but the number of reuses was limited by leaching of palladium into the reaction medium.



Equation 6. Heck reaction of acrylamide with iodobenzenes Zhang et al. using their polystyrene supported palladium catalyst.[47]

Dell'Anna et al. have reused a polymer-supported palladium catalyst for Heck reactions six times with low metal leaching.[48] This heterogeneous catalyst was prepared by AIBN-initiated radical polymerization of ethylene glycol dimethacrylate (EGDMA) and ethyl methacrylate (EMA) followed by metallation of the resulting polymer with palladium. The homogeneous version of this polymer-supported catalyst is shown in Figure 7 along with the co-monomers EMA and EDGMA. This catalyst does not contain phosphine ligands and, in the presence of sodium or potassium acetate, can be used in air in wet solvents.

The coupling of bromobenzene and styrene at 160°C in the presence of N,N-dimethylglycine (DMG) was performed six times at a Pd:aryliodide ratio of 1:1000 with little loss in activity. The DMG additive increased the activity and selectivity in the Heck reaction. The turnover frequency (TOF) the polymerized catalyst was 200 h^{-1} with DMG present and 167 h^{-1} without. The leaching of this catalyst took place in the presence of phosphine ligand while negligible metal content was found in the mother liquor of the phosphine-free system.

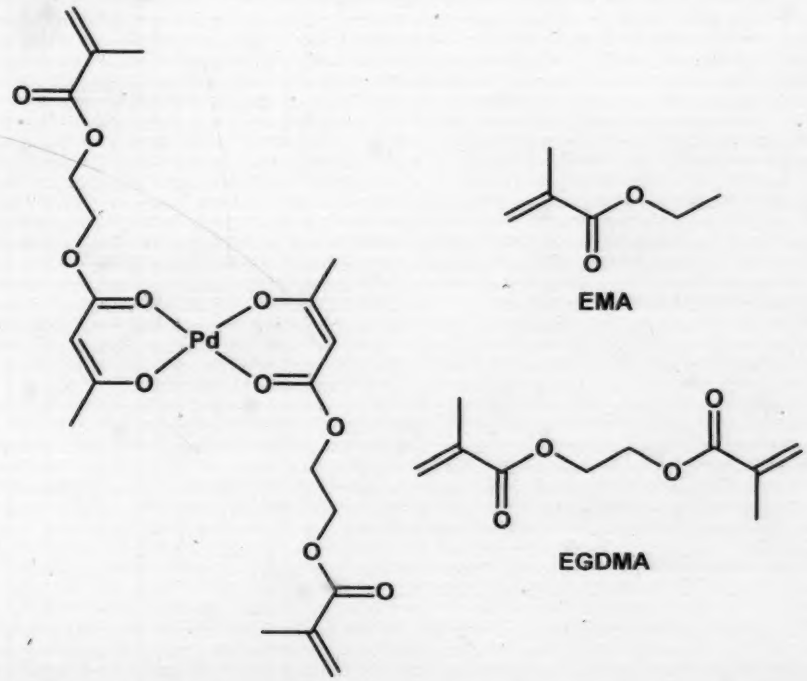


Figure 7. Homogeneous palladium catalyst used by Dell'Anna et al. used for the Heck reaction of aryl iodides and various alkenes. EMA and EGDMA were co-polymerized prior to metallation with Pd to form the polymer supported catalyst used.[48]

A highly cross-linked palladium-phosphine catalyst for Heck reactions was synthesized by Yamada et al.[49] Poly{dichlorobis[(N-isopropylacrylamide)$_5$-*co*-(4-diphenylstyrylphosphine)]} palladium (PdAS-V), shown in Figure 8, was prepared by

AIBN-initiated radical polymerization of 4-diphenyl-styrylphosphine and of *N*-isopropylacrylamide in a 1:6 ratio followed by metallation of the resulting polymer with $(NH_4)_2PdCl_4$. This catalyst was used in a series of Heck reactions between aryl iodides and acrylates, styrenes, or acrylic acids. This catalyst was recycled 5 times without loss in activity and reached a TON of 1 150 000 and a TOF of 12 000 h^{-1} with a 92% yield in the coupling of phenyl iodide and vinyl acetate in toluene. Figure 9 shows Resveratrol, a promising antitumor agent and cardiovascular disease inhibitor. This molecule was successfully synthesized with the PdAS-V catalyst in higher yield and in fewer steps than the commercially produced variety.

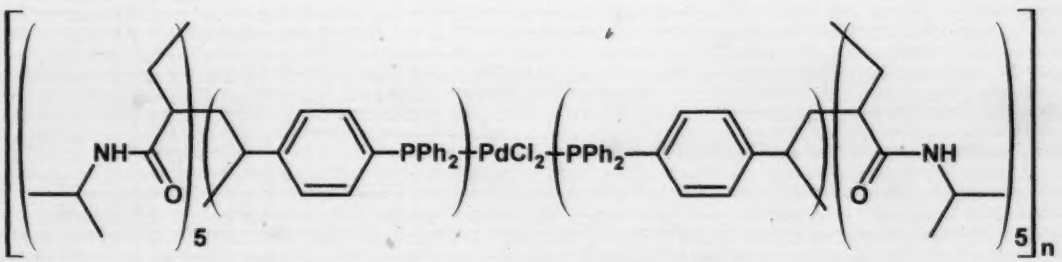


Figure 8. PdAS-V catalyst used by Yamada et al. for Heck reactions of aryl iodides and acrylates.[49]

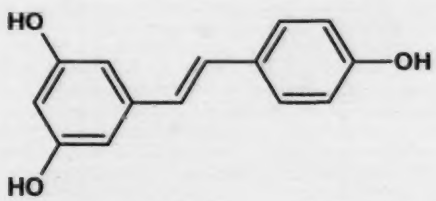
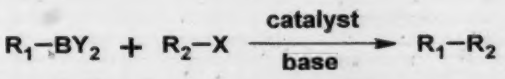


Figure 9. The structure of the antitumor agent and cardiovascular disease inhibitor Resveratrol.

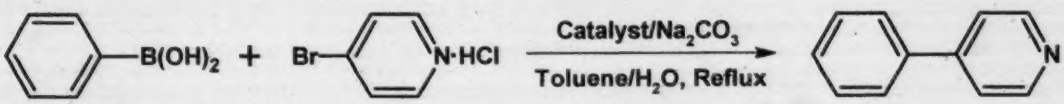
Suzuki reactions are the coupling of organoboranes and aryl halides by a palladium (0) catalyst, as shown in Equation 7 organic molecules. Biaryl molecules are used in pharmaceuticals, herbicides, and natural products as well as nanomaterials such

as conducting polymers, molecular wires, and liquid crystals.[50, 51] The organoboranes used are air and moisture stable with relatively low toxicity.



Equation 7. Suzuki coupling reaction; the coupling of organoboranes and aryl halides. X = halide or triflate. The borane can be a boronic acid or boron-esters and the catalyst is a Pd(0) species.

Fenger et al. prepared a radical initiated polystyrene-phosphine co-polymer metallated with palladium salts.[20, 21, 24] The resulting palladium polymers catalyzed the coupling between phenylboronic acid and 4-bromopyridine shown in Equation 8. The reaction was performed by the catalyst up to 5 times with no decrease in activity. In some cases, the catalyst became more active after the first use was carried out.



Equation 8. Supported palladium catalyzed Suzuki coupling reaction between phenylboronic acid and 4-bromopyridine carried out by Fenger et al.[24]

Some (0.6%) of the initial Pd leached into the reaction mixture per run. Catalysts were found to be stable in air for over a year at room temperature as opposed to the conventional catalyst $Pd(PPh_3)_4$ which is heat and air sensitive. Other bromoaromatics, such as 4-bromoaniline, 3-bromoquinoline and 4-bromoacetophenone, were also tested with varying degrees of success. The results were comparable to, or better than, the homogeneous catalyst reaction.

Another polystyrene-supported catalyst was used for Suzuki reactions by Cammidge et al.[22, 52] This polymer, however, was formed by the co-polymerization of

homogeneous metal-containing catalyst, shown in Figure 10, polystyrene, divinyl benzene and AIBN. The resulting polymer catalyzed the reaction of *p*-bromoanisole and phenylboronic acid and had a better yield, 76-81%, than the homogenous analogue, 55%. Varying the catalyst loading between 0.5 and 5% also gave similarly high yields. The catalyst was recovered and reused 5 times with no loss in activity and 1 ppm of leached metal in the crude reaction mixture on the first reaction, down to 0.1 ppm upon reuse.

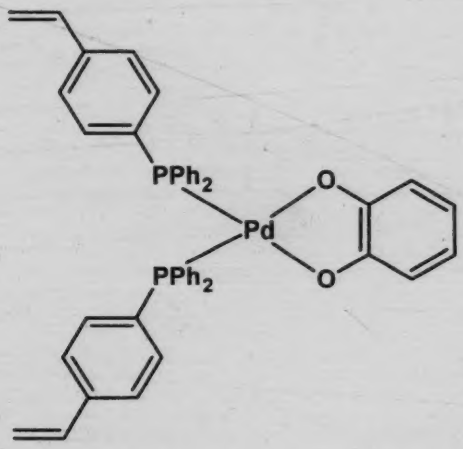


Figure 10. Catalyst monomer used by Cammidge et al. for the Suzuki coupling of *p*-bromoanisole and phenyl boronic acid.[52]

Phan et al. have designed a salen-type Pd complex immoblized on a Merrifield resin for a flow-through Suzuki reaction system.[53] Merrifield resin is a styrene-chroromethylstyrene copolymer that is cross-linked with 5% divinylbenzene. The Pd-salen complex was grafted onto the resin to form the supported catalyst shown in Figure 11. This phosphine-free system was used in the cross-coupling of various aryl and heteroaryl bromides with phenylboronic acid at elevated temperatures. The loading of the resin was 0.2 mmol Pd/g resin and the temperature of the column was achieved by

submersing in a water bath at 100°C. Conversion of up to 77% was attained for the coupling of aryl bromides and phenyl boronic acid, and up to 91% was reached for heteroaryl bromides coupled to phenylboronic acid.

In addition to the above C-C bond formation reactions, rhodium catalysts came to our attention as well as a large number are present in literature. Examples of these in recent literature include immobilized reusable catalysts being employed successfully. Recycled rhodium catalysts are used in hydrosilylation,[21, 23] hydroboration, the reduction of aromatic ketones, polymerization,[22] carbonylation,[23] and cyclopropanation[54]. Hydrogenation, hydroformylation, and asymmetric isomerisation are three reactions which use rhodium-based catalysts in industrially significant reactions and so will be expanded on herein.

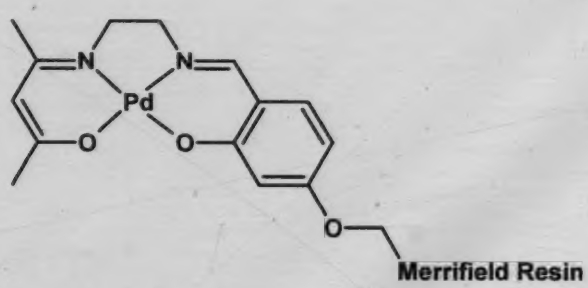


Figure 11. Merrifield resin-supported palladium catalyst used by Phan et al. in the Suzuki coupling of heteroaryl bromides and phenylboronic acid.[53]

Hydrogenation by transition metal catalysts is a fundamental synthetic method for introducing asymmetry to molecules and is used widely in industrial chemical synthesis.[55, 56] Immobilization of these catalysts for reuse will greatly impact both industrial and academic organic synthesis.[11, 18, 20-22, 26, 57-61] BINAP is one of the most successful chiral ligands used and is a convenient choice to immobilize for polymerized catalysts, as stated above in the work by Ralph et al.[3, 4, 13, 14, 62]

Pu has synthesized a rigid BINAP-derivative co-polymer with 1,4-dibromo-2,5-dialkylbenzene, the polymer is shown in Figure 12.[11, 63] The phosphine is first polymerized by Suzuki coupling followed by complexation with rhodium. This polymerized catalyst gives >95% conversion for the reduction of dehydroamino acid derivatives and enantioselectivities of 40 to 75% with a substrate to catalyst ratio of 50:1. As well, using a ruthenium-based catalyst using the BINAP derivative polymer in the presence of (*R,R*)-diphenylethylenediamine, the reduction of methyl aryl ketones was performed with up to 99% conversion and 92% *ee* with 0.5 mol % Ru and 0.2 mol % potassium t-butoxide. The catalyst was filtered and reused up to two times with no loss in activity or enantioselectivity. The polymer synthesized by Pu shares characteristics with the polymer synthesized by Ralph et al. with N-BINAP, shown in Figure 2, though the method of metallation and resulting structure differ. Pu et al. report that a well defined structure results from their polymerization which would suggest a linear repeating structure rather than the 3D-framework formed by Ralph et al.[13]

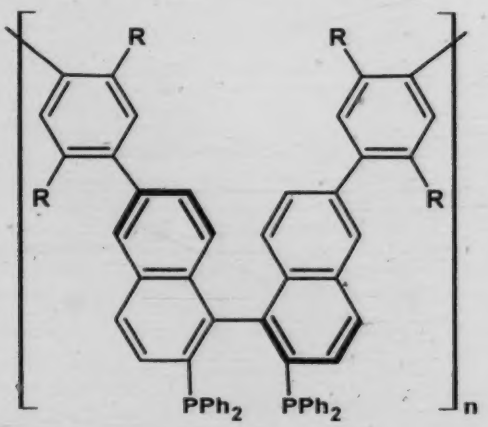


Figure 12. (*R*)-BINAP derivative polymerized with 1,4-dibromo-2,5-dialkylbenzene by Pu. The ligand is coupled to rhodium for the reduction of dehydroamino acid derivatives and methylarylketone.[63]

Hutchings et al. prepared a rhodium catalyst by ion exchange of [{(*R,R*)-Meduphos}Rh(COD)]BF_4 with acidic (H^+)Al-MCM-41 resulting in [{(*R,R*)-Me-Duphos}Rh(COD)]-Al-MCM-41.[59, 64] (*R,R*)-Meduphos is shown in Figure 13. The molecular sieve Al-MCM-41 is a mesoporous material useful in supporting catalysts due to its high surface area.

Enantioselectivities and activites reported are excellent for the asymmetric hydrogenation of dimethyl itaconate, Equation 9, >99% *ee* and >99% conversion (substrate/Rh = 250:1, 1h) over the first 5 reuses. By the eighth reuse, after a 1h reaction time, 99% conversion and 95% *ee* were obtained. A substrate/Rh ratio of 5000:1 was also carried out and achieved 98% conversion and 97% *ee* over 1 h in the first run and obtaining 97.5% conversion and 94% *ee* over 12 h by the third use.

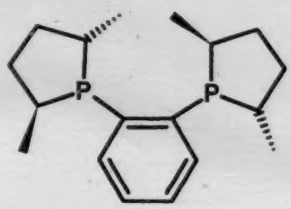
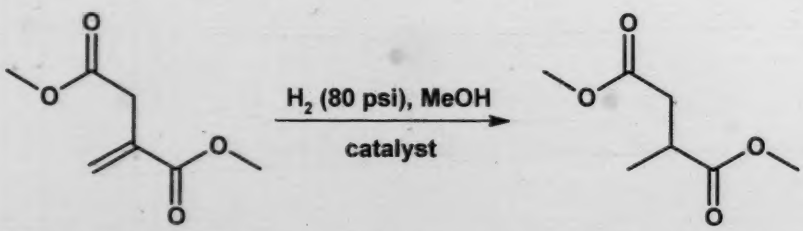


Figure 13. (*R,R*)-Meduphos, the phosphine ligand used by the group of Hutchings in their immobilized rhodium hydrogenation catalyst.[64]



Equation 9. Hydrogenation of dimethyl itaconate by [{(*R,R*)-Meduphos}Rh(COD)]-Al-MCM-41, a reusable rhodium catalyst, reported by the group of Hutching.[64]

Millions of tons of hydroformylation products are produced by industry each year for application in products such as polymers, detergents, plastics and cosmetics, among

others. [20, 21, 23, 65-68] Due to its widespread use, hydroformylation is another area in which immobilized catalysts would have a great impact. Stille et al. have immobilized derivitized DIOP (DIOP = 4,5-Bis(diphenylphosphinomethyl)-2,2-dimethyl-1,3-dioxolane) using styrene and divinyl benzene with AIBN.[21, 69] $[Rh(CO)_2Cl]_2$ and $HRh(CO)(PPh_3)_3$ were added to separate batches of the supported ligand for metallation. The resulting polymers gave comparable results between the two supported catalysts, shown in Figure 14, and the homogeneous analogue.

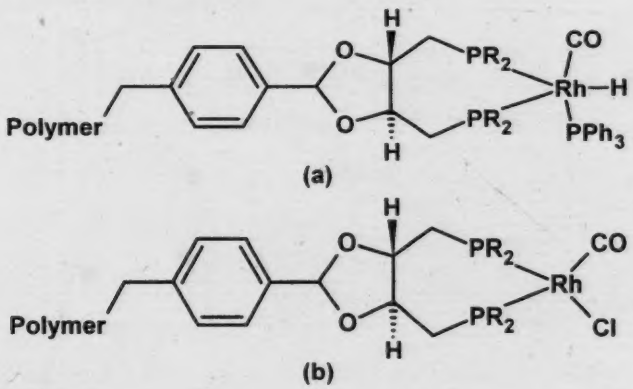
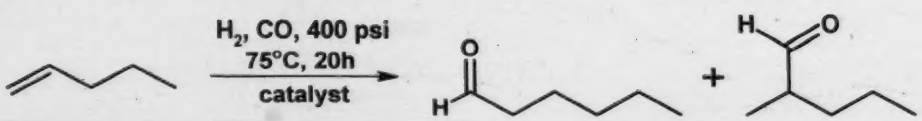


Figure 14. Immobilized DIOP-Rh catalysts used for asymmetric hydroformylation reactions by the group of Stille.[69]

The catalyst was reused 3 times in the asymmetric hydroformylation of 1-pentene, shown in Equation 10, at 1% Rh with no loss in regioselectivity. However, the reaction conditions required for maximum optical yields resulted in low activity of the catalyst. The polymer supported catalysts used also showed a 2 to 3 fold increase in branched aldehyde formation when compared to the homogeneous catalyst, though the source of this increase was not reported.



Equation 10. The hydroformylation of 1-pentene by the polymerized rhodium catalyst synthesized by Stille et al. with a branched to linear ratio of up to 0.98 on three reuses.[69]

Isomerization of natural products is a key step in the formation of many molecules in the fragrance and flavour industry such as (+)-citronellal and (-)-menthol.[70] Chapuis and co-workers prepared two polyethylene glycol-polystyrene supported BINAP ligands from derivitised TentaGel® resins and di-hydroxy functionalised BINAP.[20, 70] TentaGel® resins consist of a low cross-linked polystyrene core upon which polyethylene glycol is grafted followed by a functionalized terminus. These resins are used for peptide synthesis, combinatorial chemistry and oligonucleotide synthesis, among other uses, and are employed in batch and flow through systems.[71]

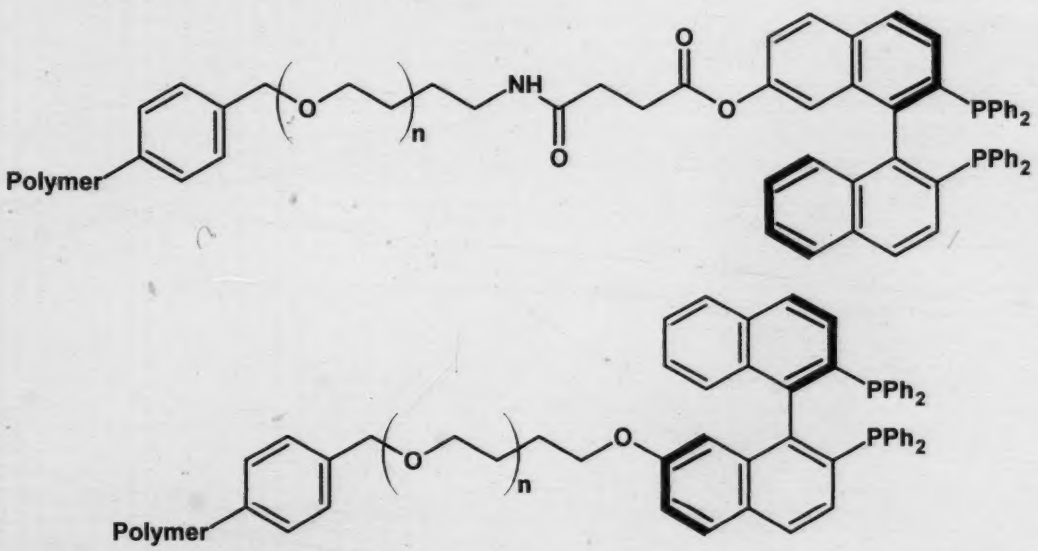
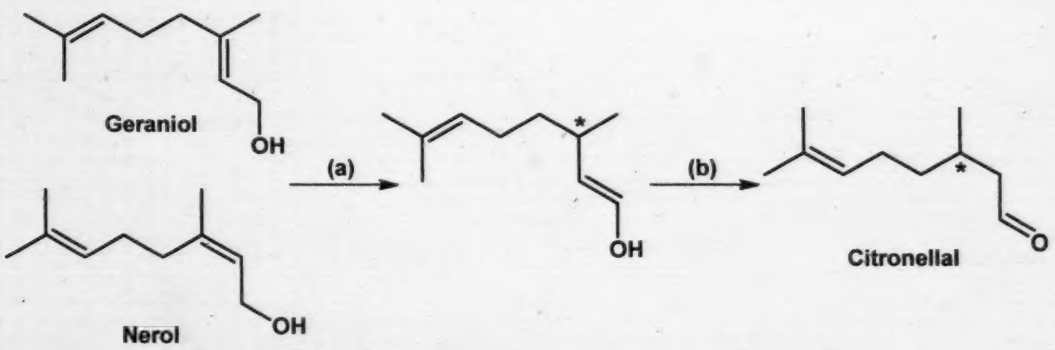


Figure 15. The polymer supported ligands used by Chapuis et al. in the isomerization of allylic alcohols. The polymer support is TentaGel®.[70]

Functionalized TentaGels® were coupled to dihydroxy-BINAP using dicyclohexylcarbodiimide and *N,N*-dimethylpyridin-4-amine as coupling agents.The polymerized ligand, shown in Figure 15, was then metallated using rhodium salts and used for the asymmetric isomerization of allylic alcohols geraniol and nerol to form citronellal. The isomerization reaction and the subsequent reaction to form citronellal is shown in Equation 11.

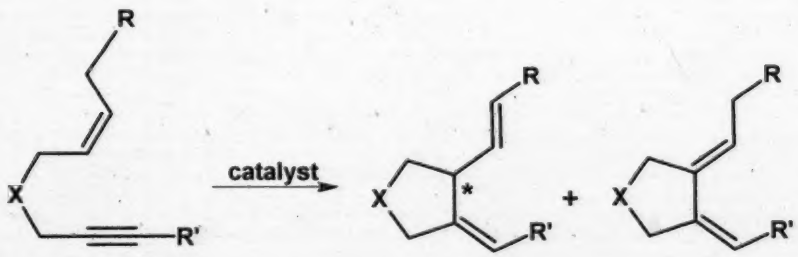
These catalysts, as well as their silica supported analogues, were found to have the same selectivity as the homogeneous analogues, though the activity was lower. The catalyst was reused 36 times at 0.25 mol % Rh and resulted in a total yield of 95% and 97% *ee*.



Equation 11. The isomerization of nerol and geraniol followed by the formation of citronellal. (a) 0.25% Rh(I) catalyst, THF, 66°C, 20h (b) AcOH, H_2O, Et_2O.[70]

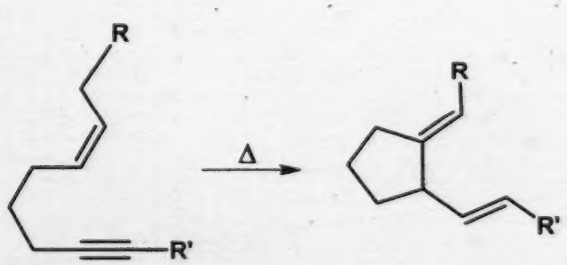
In the course of searching for suitable reactions for this study, the rhodium-catalyzed enyne cycloisomerization by Hashmi et al., shown in Equation 12, came to our attention.[72] The chiral product formed with the functionality present was promising for the construction of complex molecules. The 1,3-diene is also formed, though our focus was the formation of the chiral 1,4-diene. The 1,3-product is a focus of other reactions, as

discussed later. The relatively high percentage of catalyst required suggests a recyclable catalyst would be ideal.



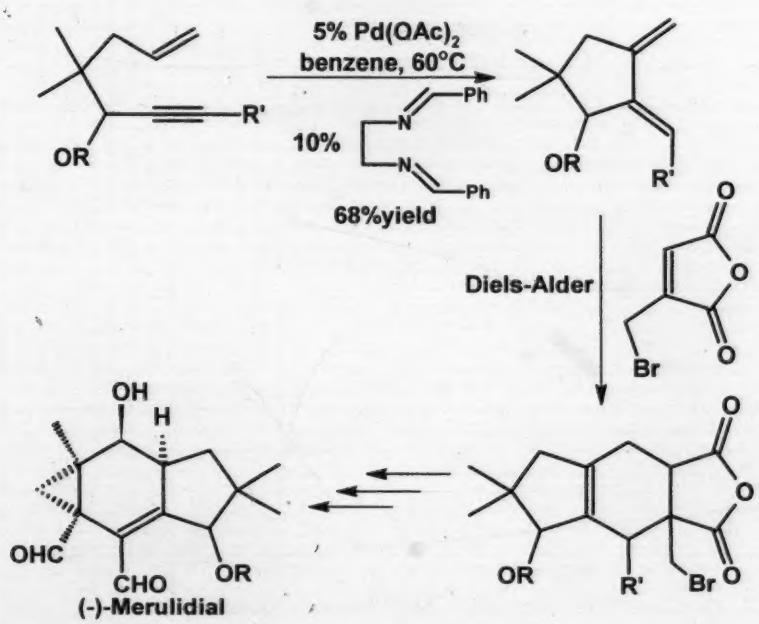
Equation 12. Catalyzed enyne cycloisomerization reaction or intramolecular Alder ene reaction. X = NR, O, CR_2.

The uncatalyzed version of this reaction, the thermal Alder ene reaction shown in Equation 13 was first studied in the 60's by Hoffmann.[73] Studies carried out by Oppolzer, Snider, and others from the 70's through to the present have used Lewis Acids in conjunction with heat to drive a different version of this reaction.[74-77] The thermal Alder ene reaction has had few uses in organic synthesis prior to the application of metal catalysis due to limitations in its scope.[73-76] Due to the nature of this reaction, a limited number of substrates can obtain a product under thermal conditions and the only product formed is the 1,4-diene.[78] The catalytic reaction, however, opens up a much wider scope of potential substrate.



Equation 13. Intramolecular thermal Alder ene reaction.

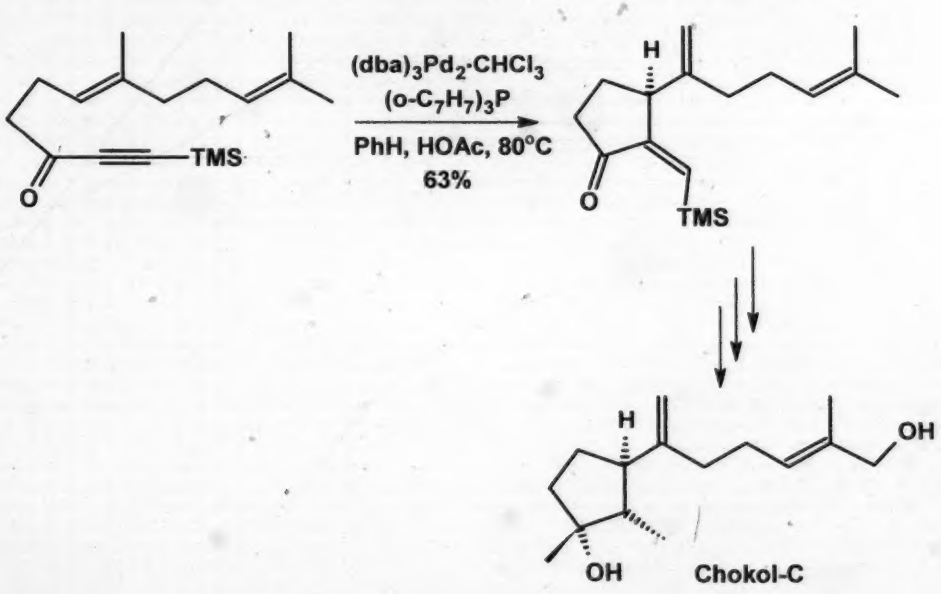
The metal catalyzed cycloisomerization reaction can be used in natural product synthesis including merulidial,[79] picrotoxanes,[80-82] cassiol,[83] saponaceolides,[84] sterepolide,[85, 86] and vitamin D metabolites [87, 88] as well as others.[89-95] The catalyzed reaction has been studied by the groups of Trost and Zhang, among others. A large portion of Trost's work on this reaction has revolved around using palladium catalysts,[78-84, 93, 96-105] though work has been carried out using ruthenium,[94, 104, 106-110] nickel[111] and nickel-chromium[104] based catalysts as well. Trost has studied reactions resulting in the primary formation of both the 1,3- and 1,4-diene products.



Equation 14. Synthesis of (-)-merulidial using catalytic isomerization followed by a Diels-Alder reaction to yield the backbone structure of the molecule.[79]

The 1,3-diene products were used for further Diels-Alder reactions resulting in multi-cyclic products,[79, 96, 98, 102] while the 1,4-products were used for the introduction of asymmetry to the molecule.[78, 80-82, 99, 105] For example, (-)-merulidial is an isolactarane sesquiterpene which is reported to have antibiotic, cytotoxic, mutagenic and antifeedant properties.[79, 85] Trost's synthesis uses a palladium-catalyzed cycloisomerization to yield the 1,3-diene. This molecule is then reacted via Diels-Alder to give the backbone of the (-)-merulidial molecule. The Alder-ene related steps of the synthesis of (-)-merulidial are shown in Equation 14.

Trost has also synthesized the antifungal compound Chokol C using $Pd_2(dba)_3 \cdot CHCl_3$ in the presence of $(o\text{-}C_7H_7)_3P$ as the *in-situ* formed catalyst for the cycloisomerization shown in Equation 15. The 1,4-diene sets part of the stereochemistry of the molecule for further reaction giving the product in 4 subsequent steps.



Equation 15. Synthesis of Chokol-C with catalyzed enyne cyclization using a palladium catalyst.[105]

Zhang's work has centred on the use of rhodium based catalysts to perform enyne cycloisomerizations.[112-117] Functionalized α-methylene-γ-butyrolactones have been synthesized in high yield and enantioselectivity.[115] These molecules are used in the synthesis of (+)-pilocarpine, shown in Figure 16, a leading therapeutic agent in the treatment of glaucoma. Equation 16 shows one of the reactions carried out by Zhang et al., the formation of a functionalized α-methylene-γ-butyrolactones.

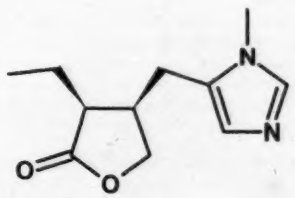
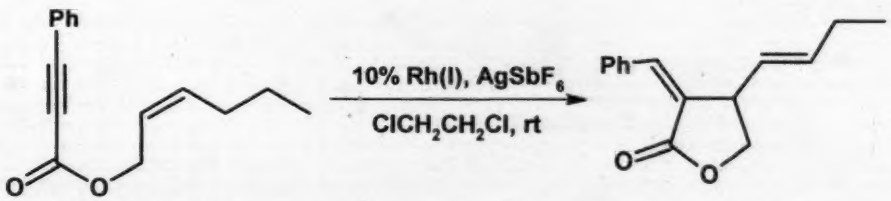
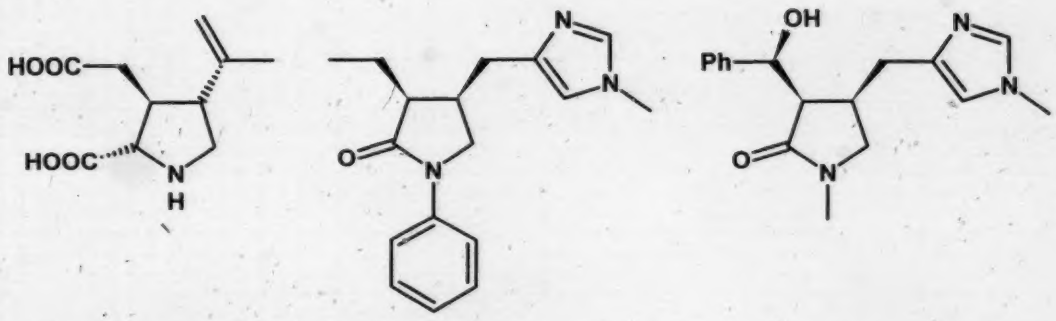


Figure 16. (+)-Pilocarpine, a glaucoma treatment whose synthesis can employ the intramolecular Alder ene reaction.



Equation 16. One of the reactions used by Zhang et al. in the study of the cycloisomerization reaction in the formation of functionalized α-methylene-γ-butyrolactones.[115]

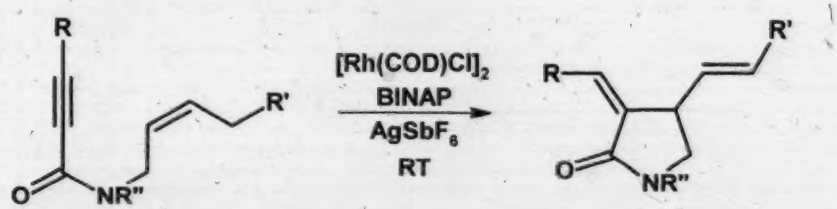
$[Rh(BINAP)Cl]_2$ with $AgSbF_6$ in dichloroethane was reacted in the presence of substrate for between 2 and 10 minutes and resulted in >90% yield and >99% *ee* for all reactions. These same reaction conditions were used in the synthesis of functionalized lactams.[113] Lactams are important organic building blocks and, when functionalized, often show biological activity or are important intermediates in the synthesis of larger active molecules. Figure 17 shows some examples of biologically significant lactams.



(+)-α-allokainic acid **isopilocarpine** **isocynometrine**

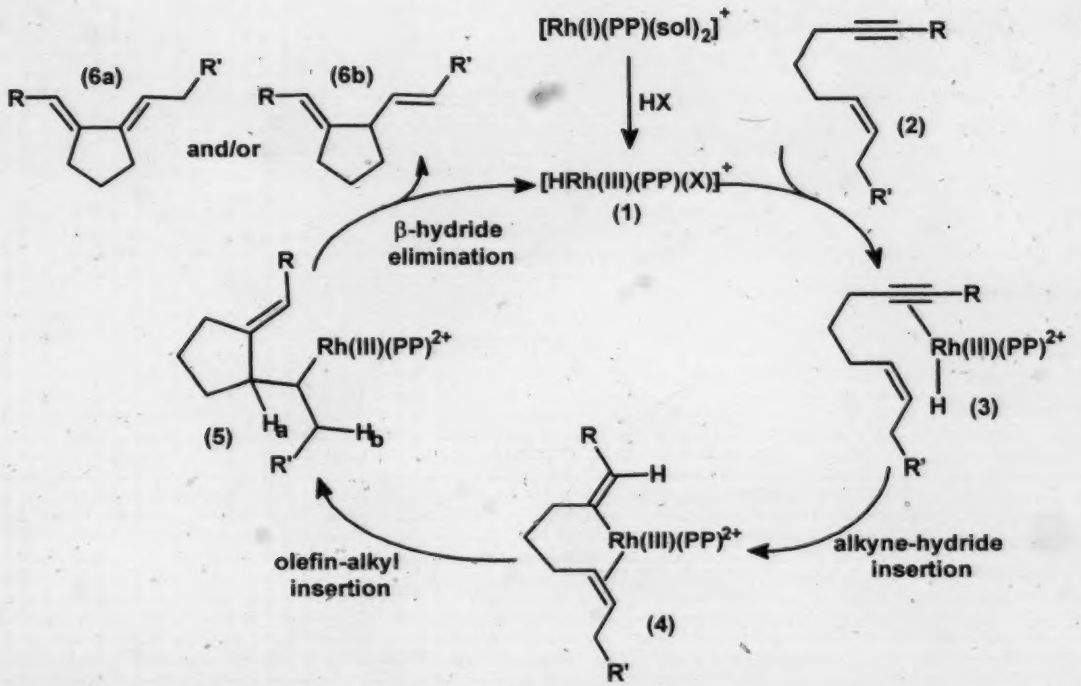
Figure 17. Examples of biologically active lactams.

Equation 17 shows the reaction studied by Zhang's group using *in situ* formed catalyst from $[Rh(COD)Cl]_2$, BINAP and $AgSbF_6$ in the production of lactams. The lactams synthesized all had >99% *ee* and >82% yield.



Equation 17. Alder ene reaction in the formation of funcionalized lactams using a Rh(I) catalyst and BINAP by the group of Zhang.[115] The ratio of substrate/Rh/BINAP/$AgSbF_6$ was 1:0.05:0.12:0.20. R = Ph, Me, *n*-C_5H_{11}; R' = H, Me, Et; R" = Bn, Me; COD = 1,5-cyclooctadiene.

One mechanism proposed for this reaction invloves the metal being protonated by an available acid to generate the active catalyst, as shown in Scheme 1.[98, 99, 102, 104] This activation step yields a hydridorhodium (III) species, **1**, and gives this mechanism its name.



Scheme 1. Hydridorhodium mechanism for enyne cycloisomerization by rhodium. The bisphosphine ligand is represented by PP and solvent molecules are represented by sol. X can be OAc^-, BF_4^- or other low-coordinating anion.

The alkyne then coordinates to the Rh centre of **1** to form **3,** followed by alkyne insertion into the Rh-H bond to produce **4**. The alkene coordinates to the metal centre followed by olefin-alkyl insertion to form the cyclopentane ring, **5**. β-Hydride elimination then forms the product, **6a** or **6b**. Depending on which hydride is eliminated, both the 1,3- and the 1,4-dienes can be formed. Newman projections are shown in Figure 18 depicting dihedral interations which determine the hydride which undergoes elimination in the final step to yield the product.

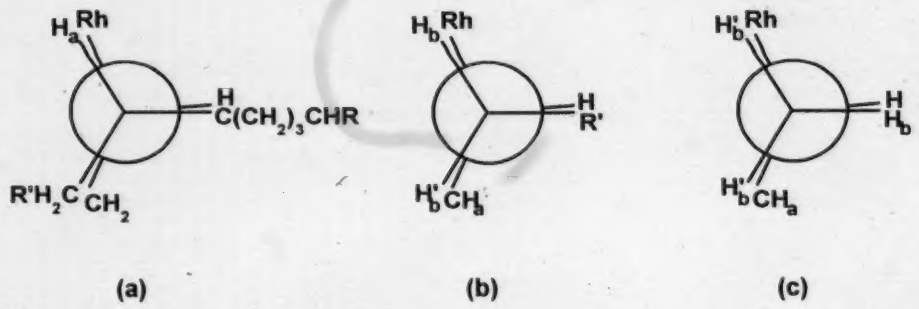
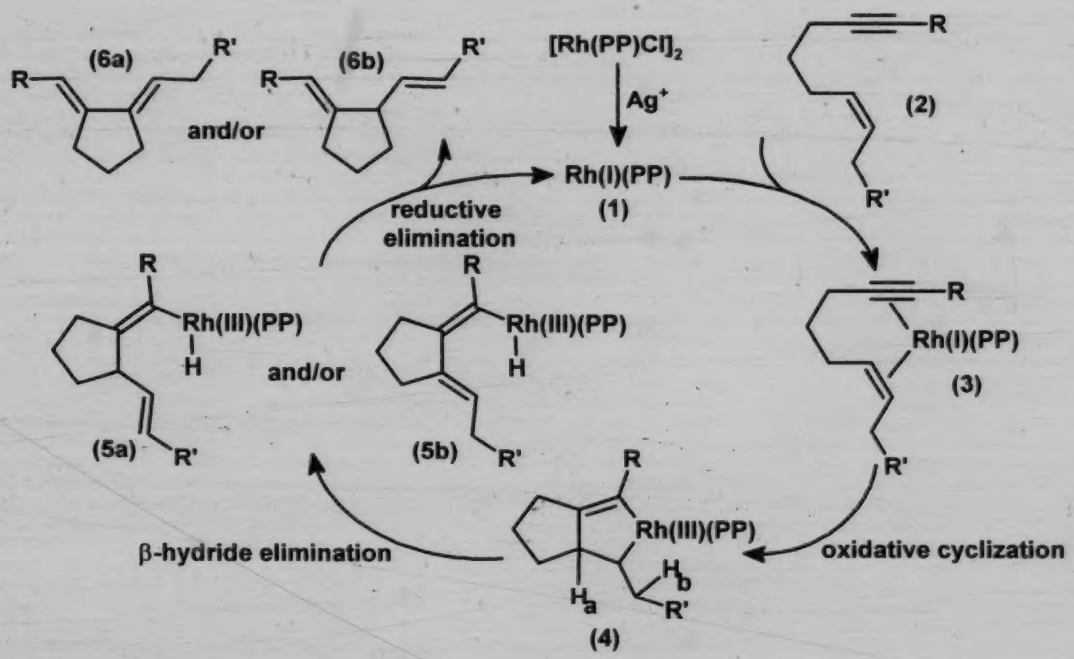


Figure 18. Newman projections of the dihedral interactions which determine the hydride eliminated in the final mechanistic step. See the text for explanation.

Figure 18a shows the dihedral interactions when H_a is aligned for elimination by rhodium while Figure 18b shows the interactions when H_b is correctly aligned. In order for H_a to be in the proper position in relation to rhodium a carbon-carbon dihedral interaction which is not present when H_b is properly aligned occurs. H_b is therefore favoured in being eliminated over H_a. Figure 18c shows the alignment of H_b' with rhodium. Again, in comparison with 18b, the H-H_b interaction in 18c is less than that of the H-R' in 18b, but the CH_a-R' interaction in 18c would greatly disfavour H_b' being aligned with rhodium. Therefore, with H_b' being disfavoured for elimination, the *trans* product of the 1,4-diene is favoured over the *cis*. In summary, due to dihedral steric interactions between neighboring alkyl groups, elimination of H_b is most likely, resulting in a 1,4-diene in the *E* configuration. Acid is not added in rhodium-based reactions carried out by Zhang et al.[112-118]

Zhang has proposed another mechanism, shown in Scheme 2, for the rhodium-catalyzed cycloisomerization reaction, again using rhodium bisphosphine catalysts.[113] The postulated catalyst of this reaction is a rhodium bisphosphine bis-solvento species, **1** which is formed after the chloro-bridged dimer is split open by $AgSbF_6$. The enyne, **2**,

coordinates to the unsaturated rhodium (I) species, **3**, followed by oxidative cyclization to give the metallacyclopentene, **4**, a rhodium (III) species. The oxidative cyclization could be a [2+2+1] addition to form the metallacyclopentane. Another possibility is that a metallacyclopropene is formed between the metal and the carbons of the alkyne and a resulting carbon insertion yields the metallacyclopentane. In either case, a β-hydride elimination gives the Rh(III)-hydride, **5a** or **5b**, and with the subsequent reductive elimination of the alkyl and H ligands, the product, **6a** or **6b**, is released and the Rh(I) species, **1**, is regenerated. This mechanism is similar to one proposed by Trost et al. for palladium-based catalysts.[98, 99, 104] Similar principles apply in the determination of regio- and stereo-isomers here as the previous hydridorhodium mechanism.



Scheme 2. Metallacyclopentene mechanism for enyne cycloisomerization by rhodium proposed by Zhang. The bisphosphine ligand is represented by PP.

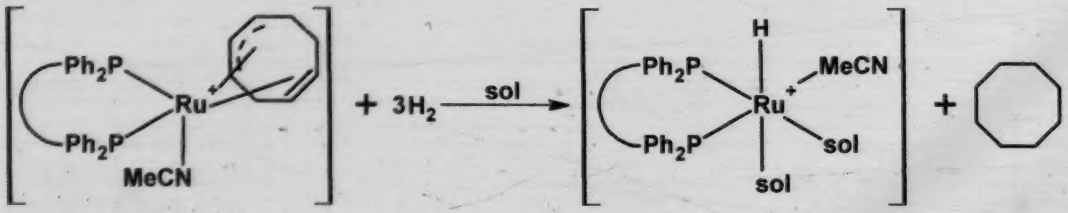
The objectives of this research were to apply the ligand system developed by Ralph et al. to prepare a catalyst-organic framework that will catalyze the intramolecular, enantioselective Alder ene reaction represented in Figure 27. This reaction was chosen because it is an enantioselective catalytic C-C bond forming reaction with products that contain useful functionality. Further, although the enantioselectivities and reaction rates reported by Zhang et al. are impressive[112-117], the required 10% loading of a Rh-BINAP catalyst is too high to make the reaction of practical value. This research aimed to create a flow-through system whereby lower than 10% loadings of catalyst were required by avoiding possible product inhibition. We note that Trost has reported that, with palladium catalysts, this reaction is product inhibited.[98] A flow-through system would be a way to alleviate product inhibition.

Chapter 2: Evaluation of Ruthenium-Based Catalysts

As discussed in Chapter 1, there are two most likely mechanisms for the cycloisomerization reaction. One, the hydrido-rhodium (III) mechanism (Scheme 1), requires a hydride ligand on the catalyst, and ideally two mutually *cis*-vacant coordination sites to accommodate the alkyne and alkene ligands. We note further that this mechanism does not involve a change in formal oxidation state. The Bergens group has developed a series of ruthenium catalysts that can be prepared in high yields that, in principle, fulfill the requirements imposed by the hydrido-rhodium mechanism on the catalyst. These are the labile solvento complexes *cis*-[Ru(H)(BINAP)(sol)$_3$]BF_4 (sol = isopropanol, acetone, methanol or THF). These complexes possess a hydride ligand and they react readily with olefin substrates via displacement of the labile solvento ligands to result in olefin-hydride insertion. Further, Trost et al. have shown that Ru-based catalysts such as CpRu(COD)Cl and [CpRu(MeCN)$_3$]PF_6 catalyze a variety of cyclization reactions related to the Alder Ene reaction studied with this project.[109, 110] We expect that the complexes used herein would be more reactive than Trost's catalysts because of the hydride and the labile solvento ligands.

Three Ru-catalyst precursors were tested: [Ru((*R*)-BINAP)(η^5-C_8H_{11})]BF_4, [Ru(MeCN)((*R*)-BINAP)(C_8H_{11})]BF_4 and [Ru(MeCN)((*R,R*)-Norphos)(C_8H_{11})]BF_4 were evaluated in 2-propanol, tetrahydrofuran, 1,2-dichloroethane, and methylene chloride as solvents. In all cases, the catalyst precursor was reacted with hydrogen gas (1 atm, RT, 8 min) first to prepare the corresponding solvento complex by hydrogenation of the C_8 ligand, as shown in Equation 18. Although it was unknown if solvento complexes such as the one shown in Equation 18 could be prepared in CH_2Cl_2, CH_2Cl_2 was evaluated as a

solvent nevertheless, with the aim of preparing a species with readily available vacant coordination sites. Cyclization of the substrates ((2Z)-3-pent-2-enyloxyprop-1-ynyl)cyclohexane (**3**) and ((2Z)-3-pent-2-enyloxy-prop-1-ynyl)benzene (**6**) were used as test reactions for this work.



Equation 18. Activation of Ru catalyst precursors by hydrogenation of the η^5-C_8H_{11} ligand. sol = iPrOH, THF, DCE, or CH_2Cl_2.

Table 1 summarizes the results. The acid $HBF_4 \cdot Et_2O$ was used in some of these screening runs in place of hydrogenation of the catalyst precursor. This was done in order to determine if the η^5-C_8H_{11} molecule needed to be present and ring slip would allow the reaction to proceed and perhaps also stabilize the active catalyst.

Table 7. Ruthenium catalysts tested in cycloisomerization reaction.

Entry	Catalyst	Substrate	Solvent	% Catalyst	Temp (°C)	Yield (%)	Time
1	[Ru(Binap)(C_8H_{11})]BF_4	3	THF	5	rt	0	4h
2			DCE	5	rt	0	4h
3[a][b]			DCE	5	60	0	4h
4			CH_2Cl_2	10	rt	0	4h
5		6	^{i}Pr-OH	10	rt	0	4h
6			^{i}Pr-OH	10	60	0	4h
7			THF	10	rt	0	4h
8			CH_2Cl_2	10	rt	0	4h
9	[Ru(MeCN)(Binap)(C_8H_{11})]BF_4	3	DCE	5	60	0	4h
10			CH_2Cl_2	10	rt	0	4h
11		6	CH_2Cl_2	10	rt	0	4h
12[a][b]			CH_2Cl_2	10	rt	0	4h
13	[Ru(MeCN)(Norphos)(C_8H_{11})]BF_4	3	CH_2Cl_2	10	rt	0	4h
14		6	CH_2Cl_2	10	rt	0	4h

Yields measured by ^{1}H NMR integration; a yield of 0% is no cycloisomerization product was observed by NMR. [a] Catalyst not hydrogenated. [b] 1 equivalent $HBF_4 \cdot EtO_2$ (to catalyst) added.

As seen in Table 1, none of the catalysts or conditions were active for the cyclization reactions. As these reactions were carried out during the screening phase, the reasons they failed were not investigated further. The most obvious explanation is, however, that the hydride mechanism does not operate for this reaction. Other reasons are possible, but as stated above, the reasons were not investigated further.

Rhodium Catalyst Testing

As discussed in Chapter 1, the groups of Zhang and Hashmi have used the dimers [Rh(bisphosphine)(Cl)]$_2$ as catalyst precursors for cycloisomerization reactions. (Many bisphosphine ligands are used such as BINAP and MeDuPhos, shown in Chapter 1, Figure 13. For a complete listing of ligands used, please see related references).[72, 112-119] Silver ions were used by these researchers in DCE presumably to remove a chloride ligand and form [Rh(diphosphine)(sol)$_2$]$^+$ where sol = weakly coordinated DCE or substrate. Heat was also used to encourage olefin dissociation using the [Rh(COD)$_2$]BF$_4$ or [Rh(NBD)$_2$]BF$_4$ (NBD = norbornadiene) precatalysts in the presence of BINAP. No studies were published on the nature of the active catalyst formed under these conditions.

Zhang and Hashmi both report cyclization of **6** and several other substrates in high yields and enantioselectivities using Rh-BINAP catalysts.[72, 112-119] For this study, [Rh(bisphosphine)(NBD)]BF$_4$ (bisphosphine = Norphos, BINAP, xylyl-BINAP and N-BINAP), were used as catalyst precursors. Both Norphos and N-BINAP ruthenium catalysts were successfully polymerized and used for catalytic reactions previously in the Bergens' group, as discussed in chapter 1.[12, 13] The NBD-Rh catalyst precursors were first activated by hydrogenation of the NBD ligands to prepare [Rh(diphosphine)(sol)$_2$]$^+$ and

related compounds that we believe are the active species in the reactions studied by the groups of Zhang and Hashmi. Figure 19 shows the structures of **3** and **6** used in catalyst screening.

Homogeneous Alder-ene reactions with [Rh(Norphos)(NBD)]BF_4, [Rh(BINAP)-(NBD)]BF_4 and [Rh(xylyl-BINAP)(NBD)]BF_4 as catalyst precursors were attempted while varying the solvent, acidity, temperature, and catalyst concentration. BINAP was used as the ligand for screening in place of N-BINAP because N-BINAP is expensive and labour intensive to prepare. We investigated the use of xylyl-BINAP with the aim of introducing a higher degree of enantioselectivity from the larger xylyl groups compared to the phenyl groups. We note that no previous Alder-ene work has been carried out using the xylyl-BINAP derivative or a rhodium-Norphos catalyst.

Table 2 shows the results from screening the rhodium-based catalysts. Acid was used in some of the screening runs, as with the Ru-based catalyst screening, in order to determine whether or not a proton was necessary to initiate the reaction. Strong acids with non-coordinating counter ions, $HBF_4 \cdot OEt_2$ and $CH_2(SO_2CF_3)$, were used to introduce the proton with minimal anion interference. Hydrochloric acid was also employed as a proton source in one of the screening reactions to contrast the other two acids used.

The Rh-Norphos catalyst (entries 15 to 21) gave no reaction for either substrate under the conditions tested.

The Rh-xylyl-BINAP catalyst (Table 2, entries 22 to 26) was active, though less so than the BINAP analog. It is likely that the xylyl-groups on the phosphorous atoms shielded the metal centre, decreasing the activity of the catalyst.

Table 8. Homogeneous rhodium catalysts tested with substrate **3** and **6**.

Entry	Catalyst	Substrate	Solvent	% Catalyst	Temp (°C)	Yield (%)	Time
15	[Rh(Norphos)(NBD)]BF_4	3	DCE	10	rt	0	4h
16[a][b]			CH_2Cl_2	10	rt	0	4h
17			CH_2Cl_2	10	rt	0	24h
18		6	THF	10	rt	0	4h
19[a][b]			DCE	10	rt	0	65h
20[a]			DCE	10	65	0	24h
21			CH_2Cl_2	10	rt	0	24h
22[b]	[Rh(xylyl-Binap)(NBD)]BF_4	6	^{i}Pr-OH	10	rt	29	1d
23			^{i}Pr-OH	10	40	10	3d
24			CH_2Cl_2	10	40	21	2d
25[b]			CH_2Cl_2	10	40	22	2d
26			CH_2Cl_2	10	rt	0	50 min
27[b]	[Rh(Binap)(NBD)]BF_4	3	THF	10	rt	64[g]	6h
28[b]			THF	10	rt	89[g]	75 min
29[c]			THF	10	rt	20[g]	70 min
30			THF	10	rt	51[g]	75 min
31			$CDCl_3$	10	rt	85[g]	40 min
32			CH_2Cl_2	10	rt	>95[g]	10 min
33[c]			CH_2Cl_2	10	rt	<10	2d
34		6	$CDCl_3$	10	rt	>95	45 min
35[a]			THF	10	rt	0	1d
36[a][c]			THF	10	rt	0	1d
37			THF	10	rt	10	2d
38[b]			THF	10	rt	10	5d
39[a][b]			THF	10	rt	10	5d
40			^{i}Pr-OH	10	40	57	2d
41[b]			^{i}Pr-OH	10	40	26	2d
42[a][b]			CH_2Cl_2	10	rt	>95	16h
43			CH_2Cl_2	10	rt	>95	30 min
44[f]			CH_2Cl_2	10	35	52	3h
45[d]			CH_2Cl_2	10	40	35	3h
46			CH_2Cl_2	5	35	80	16h
47			CH_2Cl_2	20	35	78	16h
48			DCE	10	rt	>95	1h
49	[Rh(N-Binap)(NBD)]BF_4	6	CH_2Cl_2	10	rt	>95	20 min

Yields measured by ^{1}H NMR integration. [a] Catalyst not hydrogenated. [b] 1 equivalent $HBF_4{\cdot}EtO_2$ (to catalyst) added. [c] 1 eq. (to Rh) $CH_2(SO_2CF_3)_{2(s)}$ added. [d] 1 eq. (to Rh) $HCl_{(g)}$ added. [e] <1 eq. (to Rh) $HBF_4{\cdot}EtO_2$ added. [f] <1 eq (to Rh) HCl added. [g] Side products present; significant amounts of compounds which are neither substrate nor product are present, lowering the yield.

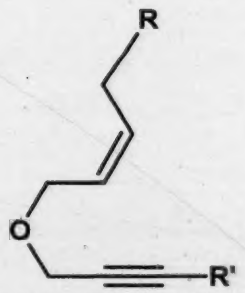


Figure 19. Structure of substrates **3** and **6**. **3**, R = CH_3, R' = Cy; **6**, R = CH_3, R' = Ph.

The Rh-N-BINAP catalyst, **10**, was active for the reaction, giving 96.6% yield in 20 minutes (Table 2, Entry 49). The *ee* of the cyclization of **6** was 95.8%, which is the same as the BINAP catalyst.[72] The *ee* was determined by gas chromatography using a Chiraldex γ-Dex column, as outlined in the experimental section.

Reaction with the Rh-BINAP catalyst (Table 2, entries 27 to 47) proceeded to some extent in all solvents and substrates though some reactions did not go cleanly. Reactions using substrate **3** in THF, for example, (Table 2, entries 27 to 30) produced many side products. It is unknown whether the reaction proceeded as expected, and the product then further reacts to yield side products, or if the substrate reacts to yield side products directly. One of the side products is an aldehyde, based on a signal in the ^1H NMR at 9.25 ppm.

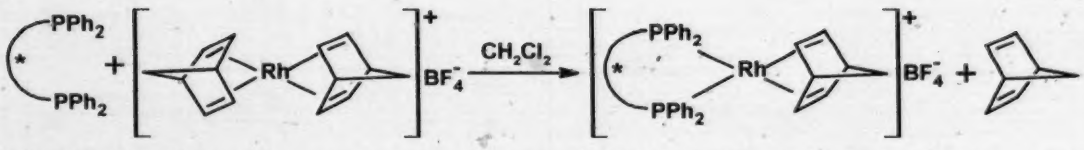
The identities of the side products were not determined for these screening studies. The objective was to determine the conditions and catalysts that provided the highest yields, rates, and *ee*'s. Several literature studies exist on the possible side products from these types of reactions. Substrate **6** reacted more quickly than with **3** and with fewer side products. Methylene chloride and 1,2-dichloroethane provided the highest yields and rates as solvents for this cyclization.

THF yields a very active catalyst, which is desired, but side product creation must be kept to a minimum in order to maximize yield. In the uncatalyzed systems more electron withdrawing substituents on the alkyne olefin give a more favourable reaction and require lower temperatures .[73-76, 120] The aliphatic cyclohexyl ring may change the electronics of the substrate enough to cause side reactions to occur in a coordinating solvent like THF. Substrate **6**, in which the cyclohexyl ring is replaced with a phenyl group, cyclized more quickly than **3** and with fewer side products.

Preparation of [Rh(N-BINAP)(NBD)]BF_4 (10)

The methodology developed by Ralph et al., as discussed in the introduction, consists of synthesizing a co-polymer using an alternating ROMP reaction. The resulting co-polymer is made up of a precatalyst monomer. The N-BINAP ligand possesses two ROMP-ready groups which yield a 3-dimensional matrix of cross-linked monomer-catalyst units, also as discussed in the introduction. The catalyst is then deposited on a solid support, washed, and used. The N-BINAP system used by Ralph for his work on Ru-based hydrogenation catalysts contained a COE:Ru ratio of 4:1. This catalyst yielded the most reuses known for a polymerized hydrogenation catalyst.

The synthesis of (*R*)-N-BINAP, shown in Equation 19 was performed by a method developed previously in this group.[13] One equivalent of the ligand was reacted with $[Rh(NBD)_2]BF_4$ in CH_2Cl_2 to give a 92% yield of [Rh((*R*)-N-BINAP)(NBD)]BF_4, **10**, as stated in the experimental section.



Equation 19. Reaction scheme showing the preparation of **10** from $[Rh(NBD)_2]BF_4$ and N-BINAP in CH_2Cl_2.

The features observed in the ^{31}P NMR spectra of both the free ligand and the ruthenium complex [Ru((*R*)-N-BINAP)Cl_2Py_2] (Py = pyridine) were not the same as those observed in the spectrum of complex **10**. Four isomers are possible from this molecule, each of which are distinguishable by ^{31}P NMR. They arise from hindered rotation around the aryl-N bond. Two C_2 dissymmetric isomers, (*R,R,R*) and (*S,R,S*), would be present as singlets, and two non-dissymmetric isomers, (*R,R,S*) and (*S,R,R*), that would be present as doublets. The (*R,R,S*) and (*S,R,R*) isomers are equivalent. At low temperatures, all of the isomers should be observed in the ^{31}P NMR spectrum as the rate of interchange between them is slower than the rate of ^{31}P relaxation. As the temperature increases, the rate of rotation about the N-aryl bond increases and the peaks begin to coalesce to the point that NMR can no longer distinguish the individual environments of the individual phosphorus atoms. As a result, the ruthenium complex has an observed singlet at high temperatures in the ^{31}P NMR. At room temperature the ^{31}P NMR of complex **10** had only one observed signal, multiplet (split by the Rh into the doublet shown in Figure 20) which corresponds to the near complete coalescence of all the isomers.

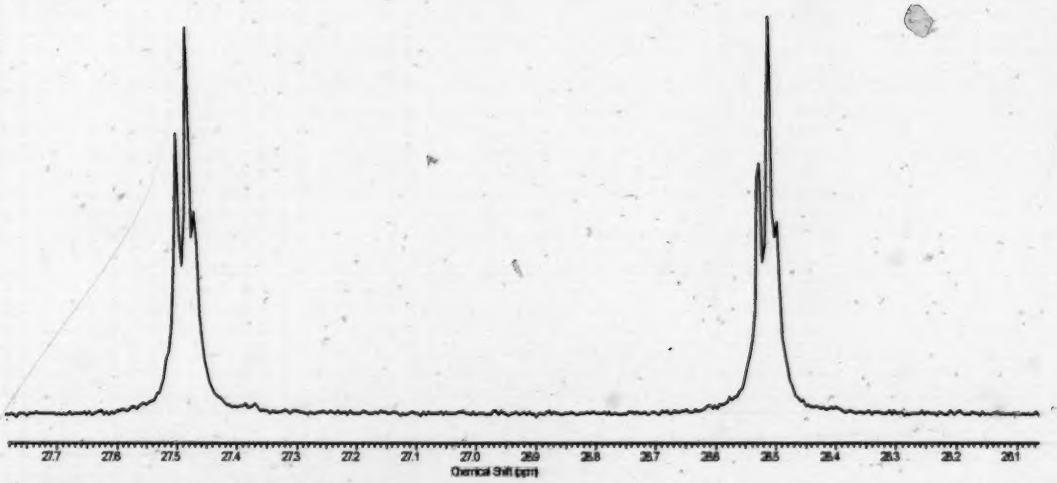


Figure 20. ^{31}P NMR of **10** at room temperature in CD_2Cl_2.

All the diastereomeric atropisomers are inequivalent on the NMR timescale at room temperature though interconversion between these isomers by rotation around the aryl-N bond is rapid and so are observed as a doublet.

Figures 21 and 22 are the ^{31}P NMR spectra of the free N-BINAP ligand and [Ru((*R*)-N-BINAP)Cl_2Py_2], respectively.[13] The Rh-complex, **10,** was dissolved in CD_2Cl_2 and observed at -40 and 20°C by ^{31}P NMR, shown in Figure 23.

As the temperature drops, all the atropisomers become visible, showing the completely reversible temperature dependence of the rotation about the aryl-N bond and the coalescence of the NMR signal.

The absence of distinguishable signals from the different isomers in the rhodium complex at room temperature led to the proposal that the electron density at the metal centre changes the aryl-N bond length and, consequently, the rotation of the norbornyl-imido groups. The Ru (II)-N-BINAP complex synthesized by Ralph has a d^6 metal centre where all the atropisomers of the ligand in the ^{31}P NMR spectrum at room temperature

can be observed. The free N-BINAP ligand has similar characteristics which suggest the aryl-N bond in the Ru-complex and the free ligand are similarly hindered (Figures 21 and 22).

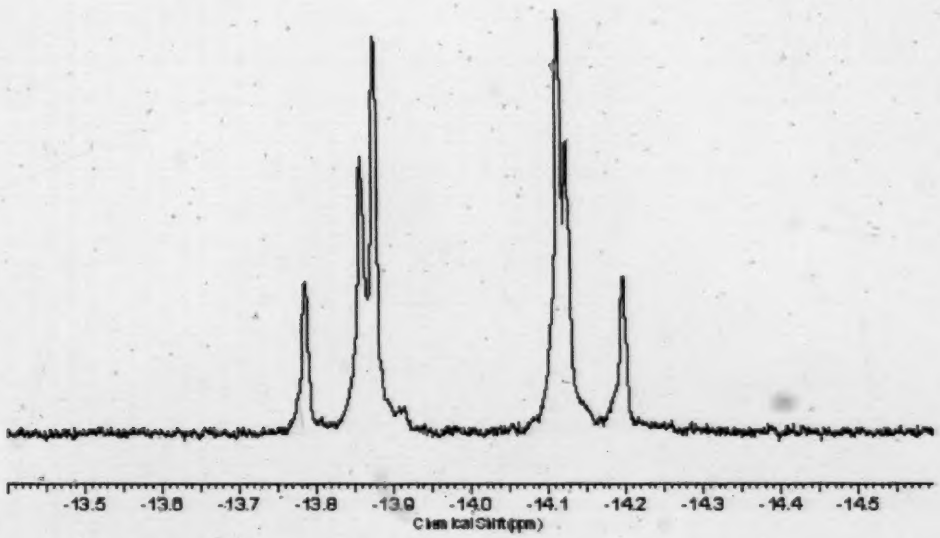


Figure 21. ^{31}P NMR of free N-Binap ligand.[13]

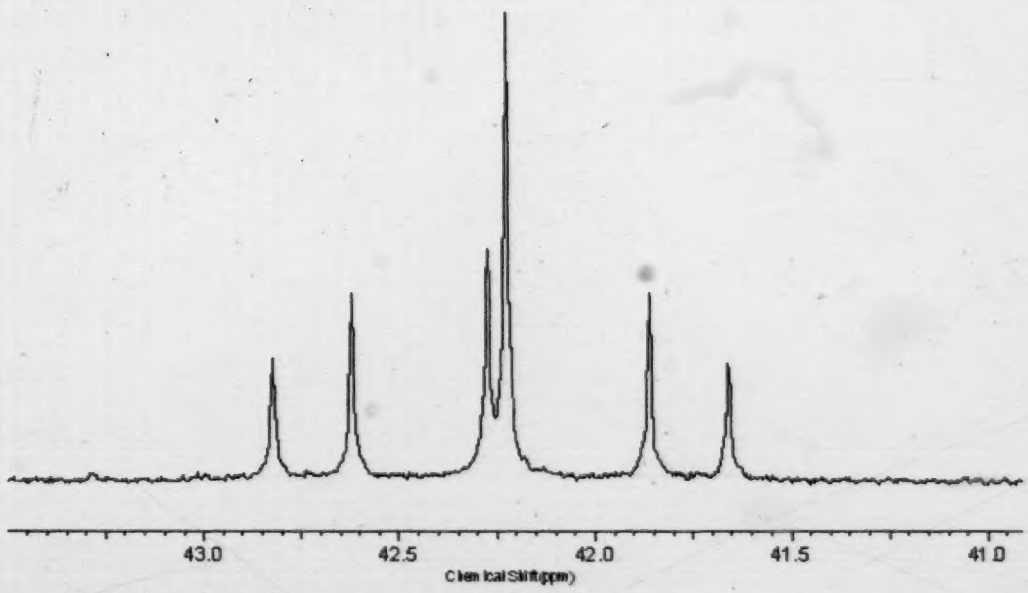


Figure 22. ^{31}P NMR of [Ru(N-Binap)Cl_2Py_2] at room temperature.[13]

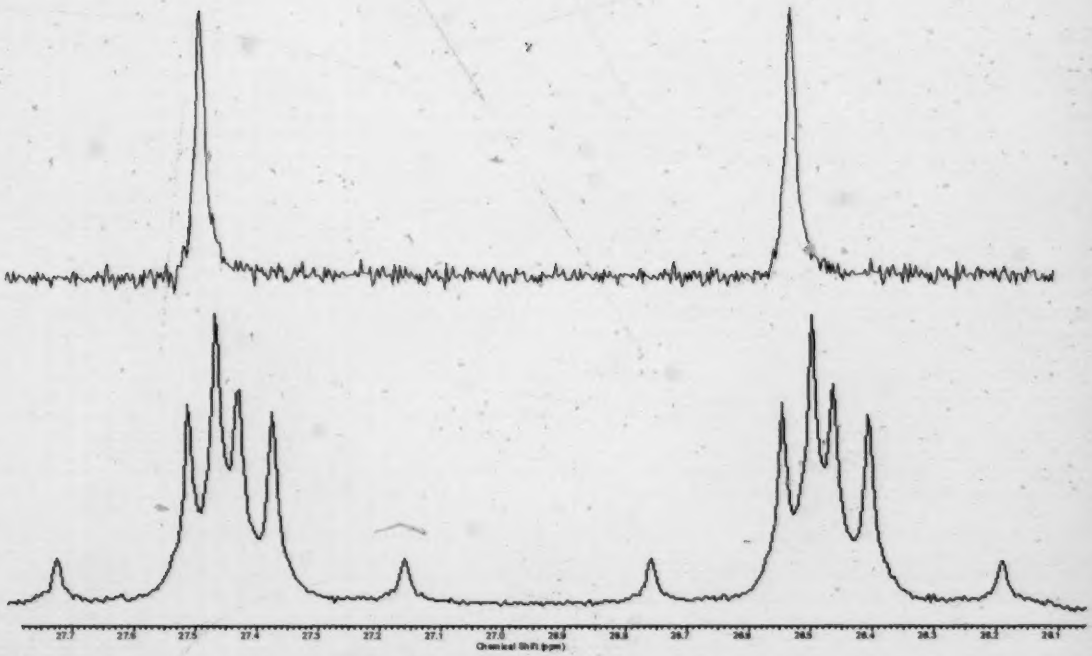


Figure 23. ^{31}P NMR of $[Rh(NBD)(N\text{-}BINAP)]BF_4$ in CD_2Cl_2 at 20 and -40°C from top to bottom respectively.

In the free ligand the aryl-N bond has restricted rotation due to sterics and partial double bond character. The lowest energy state is realized when a balance is reached between the nitrogen and the carbonyls being conjugated with the naphthyl system and steric interactions inhibiting conjugation. The relative position of the norbornyl-imido groups to the central BINAP core results in the different atropimers.

Conjugation is present from the nitrogen and carbonyls through to the metal atom. The nitrogen atom has a lone pair which can donate into either the carbonyl orbitals or the naphthyl ring π-system. The naphthyl π-system can interact with the phosphorous atoms' low level p and d orbitals. The metal d orbitals also interact with the phosphorus atoms' low level p and d orbitals. The amount of back-bonding from M to P is dependant upon the electron density at the metal centre. The Ru-centre in Ralph's complex does not

backbond enough to reduce the N-aryl double bond character to allow rotation around the N-aryl bond at room temperature. The d^8 Rh-complex, however, with more electron density at the metal, does affect this aryl-N bond length more significantly. The higher metal electron density has a higher back-bonding ability to the ligand. The higher electron density in the naphthyl system due to the back-bonding allows the nitrogen aryl bond to obtain a lower double bond character, lengthening the aryl-N bond, and allowing for a more free rotation of the nobornyl-imido groups. The lengthening of this bond also leads to lower steric effects hindering rotation. The aryl-N bond in the ruthenium complex has a more double bond character leading to decreased rotation, higher steric influence and the observation of all 4 isomers at room temperature. It is surprising that the aryl-N bond is reacting to changes in M-P interactions 7 bonds away. The delocalized electron density results in the metal being able to affect more distant bonds due to the extended molecular orbital overlap of all the atoms from the nitrogen through to the metal. Variable temperature NMR studies of free ligand, Ru, Rh and Pt compounds are underway to determine and compare the energy for rotation in these compounds.

Polymerization of [Rh(N-BINAP)(NBD)]BF_4 (10)

The first attempted polymerization of **10** used a COE:Rh ratio of 4:1 and 5% first generation Grubbs' catalyst in CH_2Cl_2 at 45°C for 18 hours. Figure 24 shows the structure formed by the rhodium complex. Sharp ^{31}P NMR signals from the monomeric catalyst give way to a broad signal in the polymerized solution indicating completion of the reaction. The ^1H NMR signals showed the polymerization was complete, as well. The use of non-deuterated solvents for subsequent polymerizations led to ^{31}P NMR being the

desired method to determine the extent of polymerization. The ^{31}P and ^{1}H spectra are given in Figures 25-28.

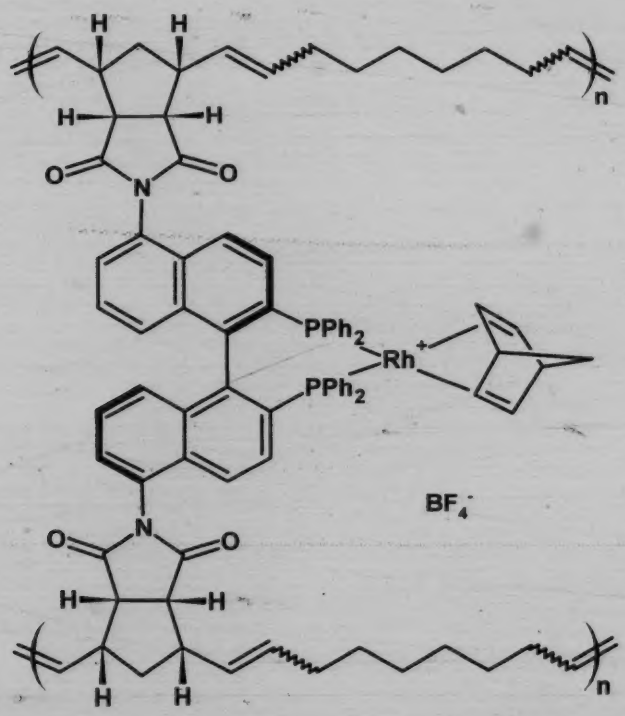


Figure 24. Structure of the rhodium(N-BINAP)/COE copolymer synthesized herein.

Figures 25 and 26 show the ^{31}P NMR spectra of the unpolymerized and polymerized spectra, respectively. The sharp doublet, due to the rhodium-phosphorous coupling, in the monomer becomes a broad, weak signal shifted slightly downfield in the polymerized form. This weaker signal is due to a large number of different phosphorous environments created by the co-polymerization reaction and by some of the polymer precipitating from the solution.

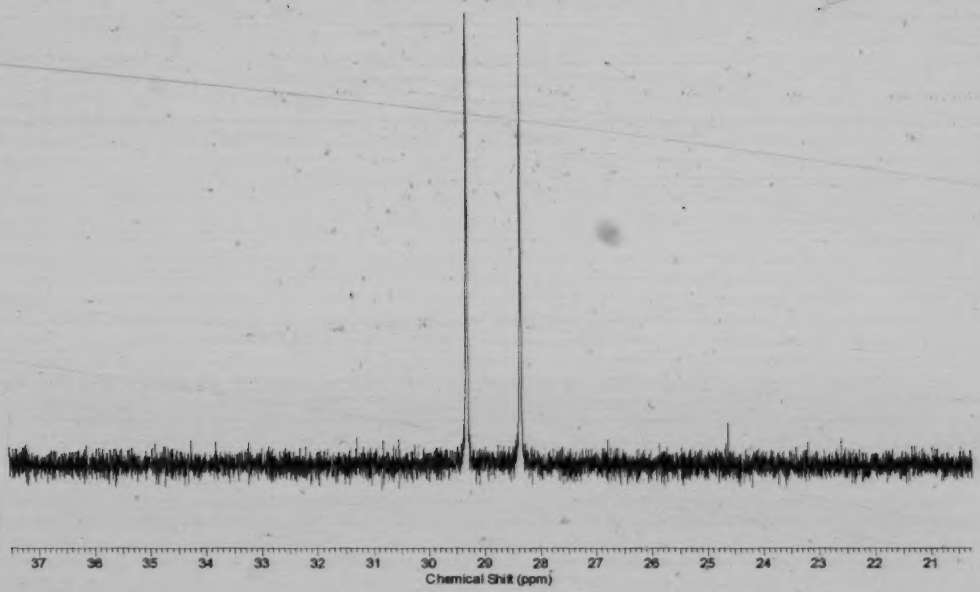


Figure 25. ^{31}P NMR Spectrum of $[Rh(NBD)(N\text{-}BINAP)]BF_4$ in the unpolymerized form. See text for analysis.

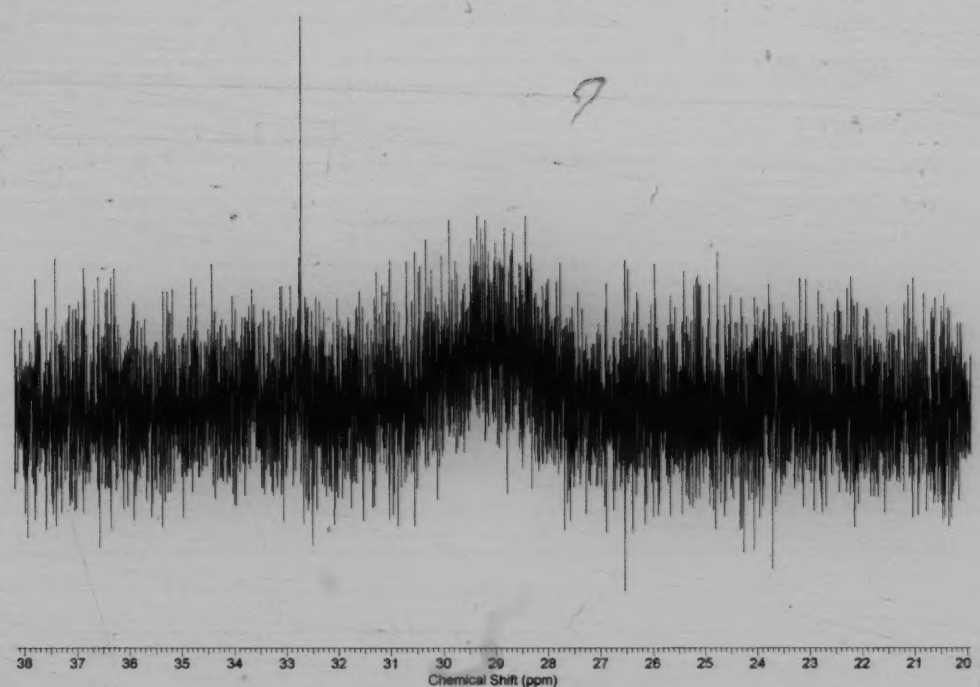


Figure 26. ^{31}P NMR spectrum of co-polymerized $[Rh(NBD)(N\text{-}BINAP)]BF_4$ with COE. The peak at 32.6 ppm is 2nd Generation Grubbs' Catalyst used for the ROMP reaction. See text for analysis.

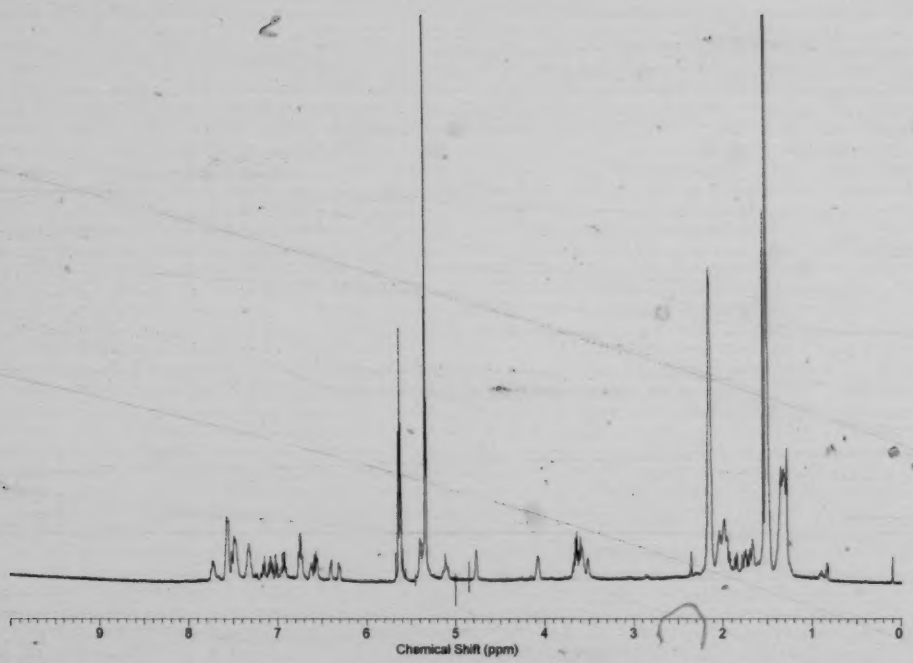


Figure 27. ^{1}H NMR spectrum of $[Rh(NBD)(N\text{-}BINAP)]BF_4$ and COE prior to polymerization. See text for analysis.

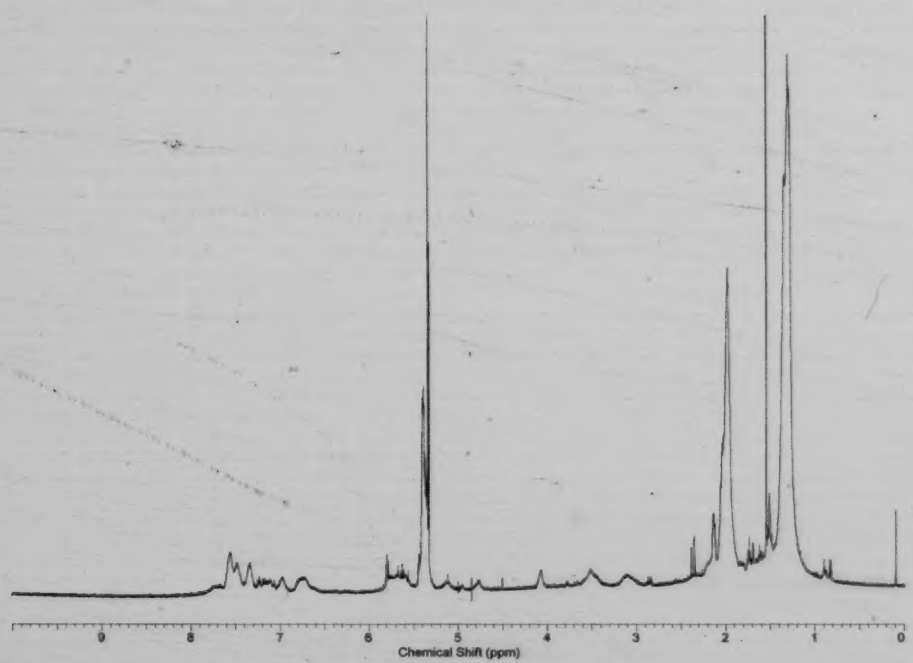


Figure 28. ^{1}H NMR spectrum of co-polymerized $[Rh(NBD)(N\text{-}BINAP)]BF_4$ with COE. See text for analysis.

Figures 27 and 28 show the ^{1}H NMR spectra of the unpolymerized and polymerized spectra, respectively. The COE signals in Figure 27 are present at 5.7, 2.2, and 1.5 ppm while the balance of the signals are due to the ligands on the rhodium complex co-monomer, [Rh(NBD)(N-BINAP)]BF_4. The COE signals are the most indicative of polymerization. COE signals are stronger due to the higher concentration, and become broader and shift upfield of the unpolymerized signal in Figure 27. The polymerized COE signals in Figure 28 are present at 5.3, 2.0 and 1.3 ppm and, with little of the monomeric COE signals present, the polymerization is nearly complete. In Figure 27 the rhodium complex signals above 6.5 ppm do not show much change other than broadening of the signal in Figure 28. The two olefin signals at 6.3 ppm and 6.4 ppm present in Figure 27 are absent in Figure 28 showing polymerization of the metal complex is nearly complete as well.

The polymer solution described above was diluted with methylene chloride to allow for a slower, more even deposition of catalyst onto the solid. The polymer was then deposited on $BaSO_4$ by slowly evaporating the solvent under vacuum. Barium sulphate was the solid used by Ralph et al. to provide mechanical support and better mass transport as the polymer is a thin film rather than a bulk mass with low surface area.

Subsequent polymers were made by changing the Rh:COE:Grubbs' Catalyst ratios. The amount of COE was increased relative to rhodium in order to permit a larger, more porous framework to allow better mass transport of the substrate to the catalyst centre. The Grubbs' catalyst was changed from First Generation to the more active

Second Generation, also shown in Equation 1 of Chapter 1, in order to accelerate the polymerization.

Table 3 shows the polymers synthesized using [Rh(NBD)(N-BINAP)]BF_4 and the time required to complete the polymerization. Entry 6 was subsequently repeated to afford supported catalyst for further cycloisomerization reactions as it took the least amount of time to complete and afforded a highly porous matrix.

Table 9. [Rh(NBD)(N-BINAP)]BF_4 polymerizations attempted. The ratio of the monomers added along with Grubbs' Catalyst, and the time to the end of the reaction are in the table.

	Ratio			
Entry	Rh	COE	Grubbs	Time
1	20	80	1.0[a]	18 h
2	20	515	1.3[a]	20 h
3	20	515	1.3[a]	18 h
4	20	2577	1.3[a]	96 h[c]
5	100	515	1.3[b]	18 h
6	20	2500	1.0[b]	<4 h

All polymers had a catalyst loading of 10 g cat/g solid. [a] First Generation Grubbs' Catalyst used. [b] Second Generation Grubbs' Catalyst used. [c] Reaction was found to be incomplete by ^{31}P NMR.

After the polymerized catalyst was synthesized and deposited on $BaSO_4$, it was reacted with hydrogen (1atm) while suspended in CH_2Cl_2. The colour of the mixture changed from a tan/orange to a brown/red colour indicating that hydrogenation had occurred to activate the catalyst. The hydrogen was removed from the system which was then treated with 10 equivalents of substrate **6**. Table 4 shows the results of the cycloisomerizations over polymerized [Rh(NBD)(N-BINAP)]BF_4.

The reactions did not go to completion in CH_2Cl_2 at 40°C. DCE was used as solvent in order to obtain higher reaction temperatures, and the literature for the

homogeneous rhodium-catalyzed reactions showed DCE as being a high-yeilding solvent for this reaction.[72, 113-118] Table 4 shows that reaction occurred in some of the trials using DCE, as it did in the methylene chloride. In both solvents, however, much longer times were required than the homogeneous reaction, and it was not possible to obtain higher than 80% yield. A dark brown colour was observed in the supernatant of all the experiments that had greater than 5% yield. In every case where reaction occurred, attempts to reuse the catalyst by washing and reuse of the solid failed to cause any cyclization.

Table 10. Polymerized [Rh(NBD)(N-BINAP)]BF_4 catalyst cycloisomerization reactions.

Entry	Polymer Ratio Rh:COE:Grubbs	Hydrogenation Time (h)	Solvent	Support	Temp (°C)	Reaction Time (h)	Yield (%)	ee
1	20:80:1[a]	0.25	CH_2Cl_2	$BaSO_4$	40	94.5[c]	39.8[d]	nd
2a	20:80:1[a]	12	CH_2Cl_2	$BaSO_4$	40	121[c]	73.0[d]	nd
2b			DCE	$BaSO_4$	80	48[c]	3.1[d]	nd
3a	20:515:1.3[a]	16	DCE	$BaSO_4$	80	90[c]	62.7	96[e]
3b			DCE	$BaSO_4$	80	121[c]	3.5[d]	nd
4	20:515:1.3[a]	16	DCE	Fe_3O_4	80	48[c]	<2[d]	nd
5[f]	20:515:1.3[a]	4.5	CH_2Cl_2	$BaSO_4$	rt	116	<2[d]	nd
6[f]	20:515:1.3[a]	4.5	DCE	$BaSO_4$	rt	116	<2[d]	nd
7[f]	20:2577:1.3[b]	3	DCE	$BaSO_4$	80	161[c]	8.3[d]	nd
8a	20:2577:1.3[b]	0.5	DCE	$BaSO_4$	45	17[c]	6.0[d]	nd
8b			DCE	$BaSO_4$	45	18	<2[d]	nd
9	20:2577:1.3[b]	16	DCE	$BaSO_4$	45	25.5[c]	3.2[d]	nd
10a	20:2500:1[b]	1	CH_2Cl_2	(solution)	45	24[c]	74.2[d]	nd
10b					45	66[c]	11.0[d]	nd
11	20:2500:1[b]	1	DCE	$BaSO_4$	45	188[c]	38.9[d]	nd
12	20:2500:1[b]	1	DCE	$BaSO_4$	80	187[c]	60.7[d]	nd
13	20:2500:1[b]	1	CH_2Cl_2	NBD Bead	45	26.5[c]	<2[d]	nd
14	20:2500:1[b]	1	CH_2Cl_2	Graphite	40	42[c]	8.0[d]	nd

[a]First Generation Grubbs' Catalyst used. [b]Second Generation Grubbs' Catalyst used. [c]Brown colour in reaction solution. [d]Yield determined by ^1H NMR. [e]Yield and *ee* determined by GC. [f]Deposited catalyst washed with methanol before use. nd = not determined.

Further, the solvent was near colourless when the washed catalysts were reused. It is most likely that the colour is due to dissolved rhodium complex in solution during the first runs, and this dissolved complex catalyzed the reaction. The solvent took on the brown colour when the supported polymeric catalyst was used for the first time and upon heating. If the supported catalyst was washed first with methanol, no colour was observed in the cyclization solution, and very little or no cyclization occurred. Methanol will not dissolve an extensively formed catalyst-organic framework made by the alternating ROMP. Methanol will only dissolve any unreacted Rh monomer, if present, or poly COE. NMR spectra, for example, of the pumped-down MeOH washings contained signals of only poly-COE in the ^{1}H NMR spectra, and no signals in the ^{31}P NMR spectra. Nevertheless, the results from the cyclization trials indicate that small amounts of unreacted Rh monomer, or perhaps short oligomers thereof, were responsible for the observed cyclizations. Washing with methanol removed these catalyst traces.

There are a few possibilities as to why the deposited catalyst does not perform the cycloisomerization reaction. First, the contact between the active catalyst and sulphate groups in the solid support could be inhibiting the reaction. The intimate contact or binding between the sulphate group oxygens and empty coordination sites on the rhodium centre could inhibit catalyst activity. Second, the activation of the catalyst precursor in the absence of substrate may be the issue. The Rh active species, $[Rh(bisphosphine)(sol)_2]^+$, may have decomposed in the time prior to substrate addition because CH_2Cl_2 and DCE were not strong enough ligands to prevent decomposition of the catalyst. To the best of our knowledge, activation of a catalyst precursor by hydrogenation has not been attempted for this cycloisomerization reaction. In the

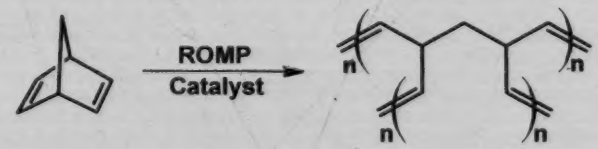
literature, the active catalyst was prepared in the presence of substrate by either olefin displacement from a catalyst precursor,[72] or reaction of a chloro-bridged dimer with silver ion (either $AgSbF_6$ or $AgBF_4$).[72, 112-118]

A third possibility is that the substrate may not be able to pass through the 3D polymer matrix to the metal centre due to the polymer being too tight or not swelled enough to allow substrate movement. By increasing the COE content of the copolymer, the spacing between metal centres is increased allowing for larger molecules to travel through the polymer, thereby accessing the activated metal.

Mass transport through the 3D polymer matrix was investigated by not depositing the matrix on $BaSO_4$ prior to the cyclization reaction (Table 4, Entry 10). Rather, the polymer matrix was left in solution after the polymerization was complete. The cyclization using dissolved polymer matrix as the catalyst was 74% complete after 24 hr, a rate dramatically less than the homogeneous reaction (100% complete after ~10 min). These results show that the polymerization of the catalyst decreases its activity.

Possible reaction inhibition caused by the solid support was studied next. Fe_3O_4 and graphite carbon were used as supports. These solids were washed with both CH_2Cl_2 and DCE followed by drying under vacuum overnight prior to deposition of polymerized catalyst using the procedure listed in the experimental section.

NBD is highly reactive towards ROMP, often reacting on mixing to form a highly cross-linked, unsaturated polymeric network, as shown in Equation 20.



Equation 20. ROMP using NBD results in a highly crosslinked, unsaturated polymer.

These networks are insoluble in most solvents and are hard, resilient materials. As ROMP is a living process, i.e. the active catalyst remains attached to the ends of the polymer, our strategy was to first prepare the poly-NBD polymeric network. This network will have the active sites, Ru-alkilidene units, embedded in and on the surface of the network. The alternating ROMP assembly between COE and **10** was then carried out using the active sites on the highly crosslinked poly-NBD beads as the ROMP catalysts. In this way, the product is an insoluble, resilient poly-NBD core with the catalyst-organic framework covalently attached to, and grown from, the surface, shown in Figure 29.

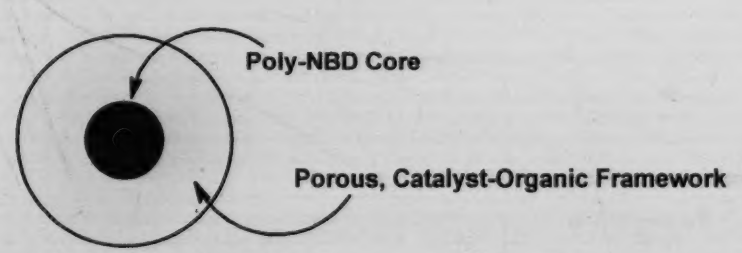


Figure 29. The insoluble NBD core is first synthesized followed by the growth of the porous catalyst-organic framework directly grafted onto the NBD core.

Further, we devised a one-pot synthesis of these supported frameworks as follows: NBD was reacted with the 2nd generation Grubbs' Catalyst (0.5 mol%) overnight in CH_2Cl_2 to ensure complete formation of the poly-NBD core and to incorporate any remaining ROMP catalyst into the surface of the core. The active sites on such a bead are likely too crowded to react with **10** directly, so the bead was first reacted with 4 equivalents of COE relative to the total amount of ROMP catalyst. This is to distance the Ru-alkilidene active catalyst from the surface of the core and to tether the active Ru-alkilidene species to the ends of linear C8 chains, reducing steric crowding around the

active sites to render them more reactive towards **10**. After a 1h reaction with COE, the cores were then reacted with **10** (16 equiv.) and COE (2000 equiv.). The reaction was left overnight to result in complete formation of the tethered catalyst-organic framework. The NBD-polymer bead (Table 4 entry 13), however, did not catalyze the cyclization reaction.

Fe_3O_4 was chosen because of its high surface area and its magnetic properties. Test experiments show that it disperses in solution with rapid stirring, but sticks to the magnetic stir bar when stirring is stopped, allowing for easy isolation between runs. The Fe_3O_4-supported catalyst (Table 4, Entry 4), however, also did not catalyze the cyclization reaction.

Finally, graphite powder was used as a solid support (Table 4 entry 14) and gave 8% yield after 42 hours. A brown colour in the supernatant was observed following the reaction. As above, it is believed that homogeneous polymer catalyst is responsible for both the brown colour of the solution and the reaction progress. This explanation would be consistent with a very small amount of catalyst performing the reaction in solution rather than the supported catalyst.

These results show that certain supports inhibit the cyclization while others allow it to occur. The active $[(\text{bisphosphine})\text{Rh}(\text{sol})_2]^+$ complex has the potential to coordinate to certain supports and be shut down. Another catalyst, $[\text{Rh}(\text{bisphosphine})\text{Cl}]_2$ (bisphosphine = N-BINAP, BINAP), was tried next due to its successful use by the Zhang and Hashmi groups for cycloisomerization reactions employing silver ions for activation in the presence of substrate.[72, 112-118]

Homogeneous Catalytic Cycloisomerization of 6 using $[Rh(BINAP)(Cl)]_2$ (11) and $[Rh(N\text{-}BINAP)(Cl)]_2$ (12)

Zhang et al. and Hashmi et al. have used the chloro-bridged dimer as a catalyst precursor in these cycloisomerization reactions.[72, 112-119] Pre-catalyts were either well defined or formed *in situ* by mixing $[Rh(NBD)Cl]_2$ and phosphine ligand. In both cases, substrate was added to the mixture prior to activation by silver salt. $AgSbF_6$ and $AgBF_4$ are equally effective in activating these catalysts. [72,112-118]

It was expected that use of the chloro-bridged dimer would avoid the solid-support problems described in the previous section. Specifically, the alternating ROMP assembly of the dimer **12** would give a catalyst-organic framework with the Rh sites as chloro-bridged dimers (Figure 30(a)). Reaction with silver ions would remove the chloride ligands, as discussed previously, to generate $[Rh(N\text{-}BINAP)(sol)_2]^+$ incorporated in the framework. As these species are held in proximity to each other by the framework, it is expected they will form bridging η^6-phenyl systems shown in Figure 30 (b). The formation of such dimmers is known for $[Rh(BINAP)(sol)_2]^+$ if sol is a weakly coordinating solvent. The dimer is a potential resting state to store the catalyst in the absence of substrate. Such dimerization is not possible in the framework made by polymerization of $[Rh(N\text{-}BINAP)(NBD)]^+$ because the Rh centres would not be held in proximity of each other.

This phenyl-bridged dimer may prevent possible coordination to the solid support and is easily formed given the proximity of the two rhodium centres upon chloride abstraction. The dimer has been shown to form in non-polar solvents and be split by more

polar solvents and more coordinating molecules, like substrate, present in the mixture.[121-125]

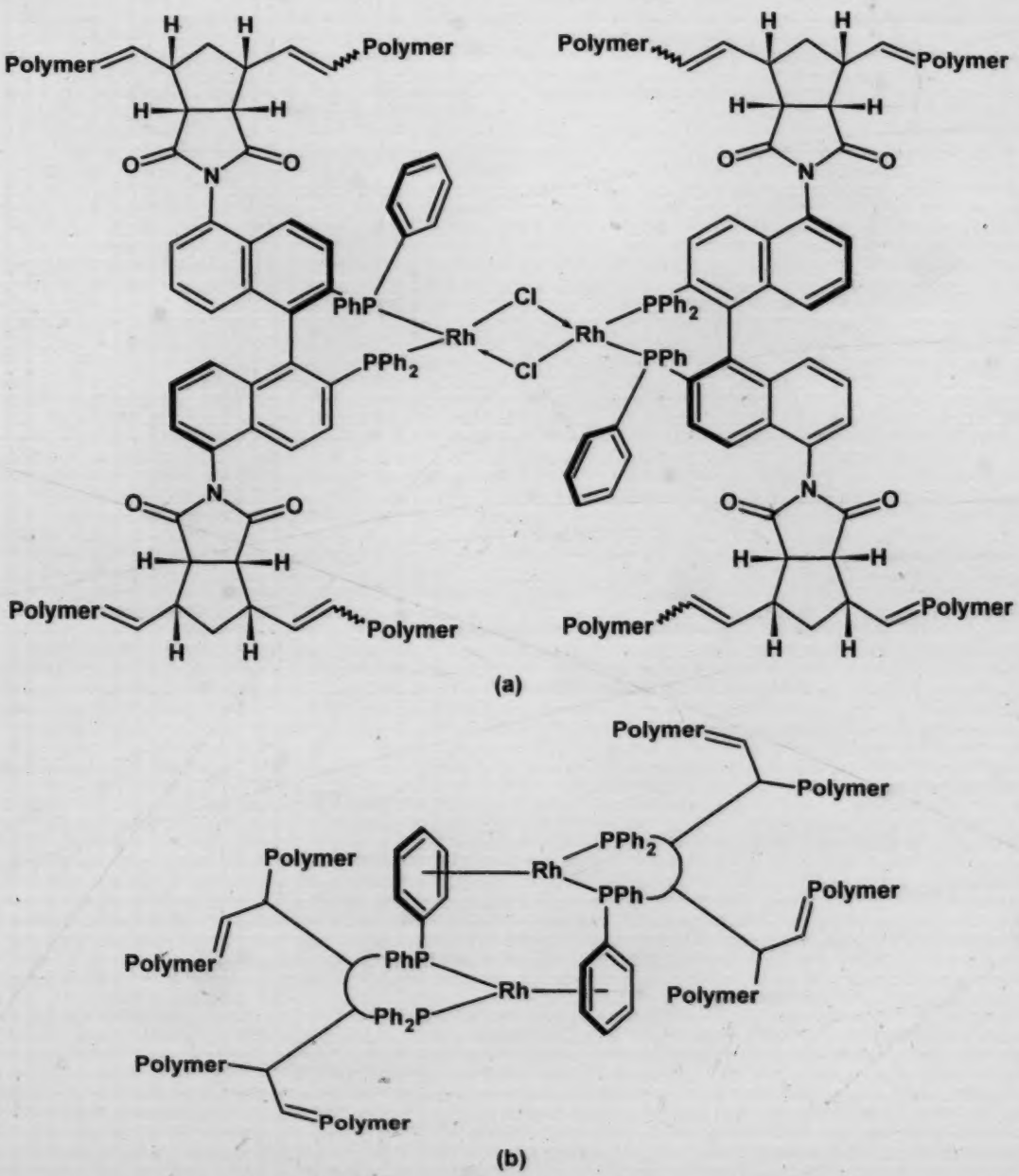


Figure 29. Possible forms of the polymerized rhodium catalyst. a) Chloro-bridged dimer prior to addition of $AgSbF_6$. b) Phenyl-bridged dimer prior to the coordination of substrate or following the cycloisomerization completion when no substrate is present. This is a possible resting state of the polymerized catalyst which can potentially be stored like this in the solid state.[121-125]

The synthesis of **11** and **12** are given in the experimental section. Table 5 shows the homogeneous reactions using **11** and **12** both in the presence and absence of various potential supports.

The pre-catalysts, with the exception of entries 1 and 10, were formed and purified prior to addition to the reaction solution with entries 1 and 10 using catalysts formed *in situ*. The rates of the reactions without solid are all similar (entries 1, 2 and 10) with all the reactions being near completion within the 10 minute period.

Table 11. Homogeneous Cycloisomerization reactions using $[Rh(BINAP)Cl]_2$ and $[Rh(N\text{-}BINAP)Cl]_2$ both with various solids present and without.

Entry	Catalyst	Solid Present	Yield (%)	Time (min)
1	$[Rh(BINAP)Cl]_2$	none	85.2[a]	10
2		none	90.6[b]	10
3		AgCl	90.1	30
4		Silica Gel	90.4	30
5		$BaSO_4$	>98	30
6		Graphite Powder	12.5	30
7		Celite	76.4	30
8		Fe_3O_4	25.4	30
9		Alumina	2.6	30
10	$[Rh(N\text{-}BINAP)Cl]_2$	none	86.0[a]	10

All reactions were carried out with 7.03 µmol catalyst, 0.141 mmol **6**, 14.77 µmol $AgSbF_6$ in 2 mL DCE. The applicable entries had 1.0 g of the listed solid added prior to addition of the substrate and $AgSbF_6$. Mixtures of solvent, solid (if applicable), catalyst and substrate were stirred for 5 minutes prior to $AgSbF_6$ addition. Yield was determined by ^1H NMR. [a] $[Rh(NBD)Cl]_2$ mixed with 2 equivalents of phosphine ligand and 2.2 equivalents of $AgSbF_6$ and mixed for 5 minutes before the addition of substrate. [b] Reaction was complete within the 10 minute period and was reacting further to make side products.

The runs done in the presence of the solids were used to determine which of the solids were compatible with the active catalyst. Reaction took place in all the mixtures where solid was present (entries 3 to 9). Reactions in the presence of AgCl, silica gel, $BaSO_4$ and Celite (entries 3, 4, 5 and 7) were nearly complete within 30 minutes, somewhat, but not prohibitively slower than in the absence of these solids. The graphite

powder, iron oxide and alumina (Entries 6, 8, and 9) did not work as well, giving considerably lower yields after 30 minutes.

Graphite powder, Fe_3O_4, and alumina were not investigated further. The next section will discuss the preparation and use of a flow-through system for this reaction using a polymer-catalyst framework made from COE and **12** and silica gel as support.

Flow-Through Column Reactors

Flow through column reactors offer a number of advantages over batch reactors. The column will avoid the need to filter the supported catalyst after each run, as is required with a batch reaction, thus reducing the time required between runs. A column reactor avoids stirring issues such as flattened stirbars, ground up catalyst and catalyst splashing up on the sides of the reaction flask, all of which can contribute to loss of catalyst or loss of reaction efficiency. Substrate solution can be passed over the supported catalyst continuously and product can be collected at the bottom, reducing the effect of product inhibition, as in this cycloisomerization reaction.[98] Substrate would only be in contact with the catalyst long enough to react and, with no final filtration necessary, product is removed from catalyst contact immediately in a column system. The catalyst does not have to be protected or have a resting state between the runs due to the continuous supply of new substrate and removal of product.

Table 6 shows the ROMP copolymerization conditions using catalyst **12**, COE, and Second Generation Grubbs' Catalyst.

Entry 1 of Table 6 was deposited on silica gel using the procedure stated in the experimental section. Silica gel was used as the support of the catalyst due to its high

surface area and as it is used in column chromatography, the reaction solution would pass easily through the column under low pressure. Solvent was left on the column in order to swell the polymer for 15 minutes prior to substrate solution addition. Swelling expands the polymer to allow the substrate access to the catalyst centres by increased mass transport through the polymer matrix.

Table 12. Polymerization of $[Rh(N\text{-}BINAP)Cl]_2$ and the times required to reach completion. Both reactions were carried out using Second Generation Grubbs' Catalyst in freshly distilled CH_2Cl_2.

	$[Rh(N\text{-}Binap)Cl]_2$	Ratio			
Entry	m (mg)	Rh	COE	Grubbs	Time
1	12.5	20	2500	1.0	16 h
2	25	10	1250	1.0	3 h

$AgSbF_6$ (2.2 equivalents to Rh) and substrate **6** (10 equivalents to Rh) were dissolved in DCE and passed through the column at a rate so that the residence time of the substrate was 60 minutes. This is twice the time required for the homogeneous reaction to be completed in the presence of solid, as determined in the previous section. The extra time was provided in order to account for mass transport through the polymer matrix on the column. After the 60 minute interval, another 10 equivalents of **6** in DCE was passed through the column. This was repeated for 5 more samples with the last sample being left on the column overnight. ^1H NMR spectroscopy showed, however, that only starting material with no product or side products formed.

Conclusion

Trost and Zhang have had success in the enyne cycloisomerization reaction in both the design of catalysts and the application to complex organic product synthesis. The

ruthenium catalysts studied herein were found to be unsuccessful in the homogeneous reactions. Rhodium catalysts were then synthesized and found to isomerize the substrate in high yield and enantioselectivity. Following the methodology developed in the Bergens group, polymerized catalysts were synthesized and cyclization reactions attempted.[13] Using several solid supports no products were detected from the reaction. This is likely due to the substrate, product or side products binding strongly to the metal centre. This would result in the catalyst becoming inactive towards further reaction and gives the results shown above.

In spite of the unfavorable results in this work, a multiply charged metal containing polymer, poly-COE-[Rh(N-BINAP)(NBD)]BF_4, was successfully synthesized using the ROMP copolymer methodology. Hydrogenation, hydroformylation and isomerization of allylic alcohols are three reactions which utilize rhodium catalysts and could be the source of a study involving the catalysts used herein.

This work has also shown that solid supports do have an influence on the reaction. The solids testing used a variety of potential supports and showed which were detrimental to the target reaction. This method allows for screening solids without polymerization and deposition of metal catalyst. An extension of this solids testing to successful polymer catalysts and the use of chiral supports may lead to further enhancement of selectivity in reactions tested.

With the large number of reactions where polymerized BINAP is used, the N-BINAP ligand may add a new dimension. The polymer properties of this ligand should be investigated and may provide an added chiral influence on enantioselective reactions. The

changing properties with metal electron density should also be investigated for possible application in materials science.

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Experimental Section

Materials and methods. Operations performed under N_2 used standard Schlenk techniques. Prepurified N_2 gas (Praxair, 99.99%) was passed through a drying train containing 3 Å molecular sieves and P_4O_{10} before use. The solvents, n-hexane (K, Ph_2CO), methylene chloride (CaH_2), tetrahydrofuran (K, Ph_2CO), and isopropanol ($Mg(O^iPr)_2$) were distilled from drying agents under nitrogen. Dichloroethane (Aldrich Chemical Co., anhydrous, Sure/Seal^{TM} bottle, 99.8%), diethyl ether, petroleum ether and ethyl acetate were used as received. Phenyl acetylene, cyclohexyl acetylene, n-BuLi, PBr_3, NaH, KH, and *cis*-2-penten-1-ol were all used as received from Aldrich Chemical Co. (*R*)-BINAP and *rac*-BINAP were used as received from Strem Chemical Co., Inc.

White reflectance $BaSO_4$ was obtained from Eastman Chemical Co., Inc. Silica gel (flash chromatography grade), Celite, graphite powder (<20 micron) Teflon, glass wool, sand were all obtained from Aldrich Chemical Co., Inc. Purified Fe_3O_4 was obtained from Fisher Scientific Company. Barium tartrate was prepared and cleaned in the lab by Corbin Ralph. All solids were washed 3-4 times with CH_2Cl_2 and dried under vacuum overnight before use.

Instrumentation. All ^1H, ^{13}C and ^{31}P spectra were measured on one of 2 instruments at the University of Alberta: a Varian Inova 400 MHz, or a Varian Unity 500 MHz spectrometer. ^1H spectra were also collected on a Varian Inova 300 MHz spectrometer. ^1H spectra were run at 299.97, 400.40 or 499.83 MHz; ^{13}C at 100.54 or 125.70 MHz; ^{31}P

at 161.84 or 202.34 MHz. ^{1}H and ^{13}C NMR chemical shifts are reported in parts per million (δ) relative to the residual solvent peak. ^{31}P NMR chemical shifts are reported in parts per million (δ) relative to an 85% H_3PO_4 external reference. All ^{31}P and ^{13}C spectra are ^{1}H decoupled. Microanalyses were performed at the University of Alberta Microanalysis Laboratory. Gas chromatography (GC) was performed on a Chiraldex γ-Dex column (30 m x 0.25 mm) fitted to a Hewlett-Packard 5890 gas chromatograph with a Hewlett-Packard 3392A integrator.

3-Cyclohexyl-2-propyn-1-ol (1). The substance was prepared by the general procedure given by Hashmi et al.[1] Under a nitrogen atmosphere 5.0 g (5.95 mL, 46.2 mmol) cyclohexyl acetylene in 40 mL absolute THF was cooled to -78°C. Then 28.9 mL n-BuLi (46.2 mmol, 1.6 M in hexanes) was added dropwise. The solution was warmed to 0°C and then 1.85 g (61.2 mmol) paraformaldehyde was added. After the solution had warmed to room temperature, it was heated to 45°C for 90 minutes. After cooling back to room temperature, the reaction mixture was poured into a solution of 15 g ammonium chloride in 100 mL of water. After separation of the phases, the aqueous phase was extracted with 15 mL diethyl ether five times, dried over $MgSO_4$, filtered, and the solvent removed under vacuum. Silica gel flash chromatography using a 1:1 hexane:ethyl acetate mixture gave the product as a yellow oil; yield: 5.91g (44.7 mmol, 98%). R_f (Hexane:Ethyl Acetate, 1:1) = 0.67; ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 1.26 - 1.66 (m, 7 H) 1.69 - 1.81 (m, 2 H) 1.81 - 1.93 (m, 2 H) 2.38 - 2.52 (m, 1 H) 4.33 (d, *J*=1.83 Hz, 2 H).

3-Cyclohexyl-2-propynyl Bromide (2). The substance was prepared by the general procedure given in literature.[1] 6.35 g (46.0 mmol) **1** in 50 mL absolute diethyl ether was cooled to 0°C. Then 0.5 mL freshly distilled pyridine and 2.18 mL (6.23 g, 23.0 mmol) PBr_3 was added and stirring continued for 4 hours at 0°C. The mixture was then poured into 50 mL saturated $NaHCO_3$ solution, extracted with 20 mL ether three times and dried over Na_2SO_4. After filtration and removal of solvent under vacuum, the mixture was purified by silica gel flash chromatography using a 2:1 hexane:ethyl acetate mixture. **2** was obtained as a yellow oil; yield: 5.67 g (30.7 mmol, 61%). R_f (Hexane:Ethyl Acetate, 2:1) = 0.96; ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 1.25 - 1.64 (m, 6 H), 1.68 - 1.93 (m, 4 H), 2.42 - 2.56 (m, 1 H), 4.01 (d, *J*=1.83 Hz, 2 H).

((2Z)-3-Pent-2-enyloxyprop-1-ylyl)cyclohexane (3). The substance was prepared by the general procedure given by Hashmi et al.[1] 2.85 mL (2.43 g, 28.2 mmol) cis-2-penten-1-ol in absolute THF was cooled to 0°C. Then 1.13 g KH was added. When no more gas was evolved, 5.67 g (30.7 mmol) **2** in THF was added. Stirring was continued at 0°C for one hour, then the solution was warmed to room temperature, washed with water and the aqueous phase was extracted with 20 mL ether three times. The combined organic phases were dried over $MgSO_4$, filtered and the solvent removed under vacuum. Silica gel flash chromatography (1:2 hexane:ethyl acetate solvent mixture) gave **6** as a yellow oil; yield 2.97 g (14.4 mmol, 51%) R_f (Hexane:Ethyl Acetate 1:2) = 0.72; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 0.91 (t, *J*=7.57 Hz, 3 H) 1.15 - 1.29 (m, 3 H) 1.29 - 1.48 (m, 3 H) 1.57 - 1.66 (m, 2 H) 1.67 - 1.76 (m, 2 H) 2.03 (pd, *J*=7.39, 1.22 Hz, 2 H) 2.28 - 2.37 (m, 1 H) 4.00 - 4.03 (m, 2 H) 4.03 (d, *J*=2.20 Hz, 2 H) 5.35 - 5.57 (m, 2 H); ^{13}C NMR (101 MHz,

$CDCl_3$) δ ppm 14.05, 20.76, 24.70, 25.80, 28.99, 32.52, 57.19, 64.28, 75.82, 90.60, 124.80, 135.74; anal. calcd. for $C_{14}H_{22}O$ (206.32): C 81.50, H 10.75; found C 81.83, H 10.79. The purity and identity of this compound confirms the identity of the previous two intermediates (**1** and **2**).

3-Phenyl-2-propyn-1-ol (4). The substance was prepared by the procedure given in literature.[1] Under a nitrogen atmosphere 5.0 mL (4.65 g, 45.5 mmol) phenylacetylene in 40 mL absolute THF was cooled to -78°C. Then 28.5 mL n-BuLi (45.5 mmol, 1.6 M in hexanes) was added dropwise. The solution was warmed to 0°C and then 1.92 g (63.9 mmol) paraformaldehyde was added. After the solution had warmed to room temperature, it was heated to 45°C for 90 minutes. After cooling back to room temperature, the reaction mixture was poured into a solution of 15 g ammonium chloride in 100 mL of water. After separation of the phases, the aqueous phase was extracted with 15 mL diethyl ether five times, dried over $MgSO_4$, filtered, and the solvent removed under vacuum. Silica gel flash chromatography using a 2:1 petroleum ether:Et_2O mixture gave **4** as a yellow oil; yield: 5.91g (44.7 mmol, 98%). The spectroscopic data were in accordance with literature.[1] R_f (Petroleum Ether:Et_2O, 2:1) = 0.33; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm = 4.53 (s, 2 H), 7.27 - 7.36 (m, 3 H), 7.43 - 7.50 (m, 2 H).

3-Phenyl-2-propynyl Bromide (5). The substance was prepared by the procedure given in literature.[1] 5.91 g (44.7 mmol) **4** in 50 mL absolute diethyl ether was cooled to 0°C. Then 0.5 mL freshly distilled pyridine and 1.88 mL (4.84 g, 17.9 mmol) PBr_3 was added and stirring continued for 4 hours at 0°C. The mixture was then poured into 50 mL

saturated $NaHCO_3$ solution, extracted with 20 mL ether three times and dried over Na_2SO_4. After filtration the mixture was purified by silica gel flash chromatography (50:1 petroleum ether: Et_2O), the solvent removed and **5** was obtained as a yellow oil; yield: 5.99 g (30.7 mmol, 69%). The spectroscopic data were in accordance with literature.(state ref. here, too) R_f (Petroleum Ether:Et_2O, 50:1) = 0.41; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm = 4.19 (s, 2 H), 7.31 - 7.40 (m, 3 H), 7.44 - 7.51 (m, 2 H).

((2Z)-3-Pent-2-enyloxy-prop-1-ylyl)benzene (6). The substance was prepared by the general procedure given by Hashmi et al.[1] 3.10 mL (2.64 g, 30.7 mmol) cis-2-penten-1-ol in absolute THF was cooled to 0°C. Then 0.706 g NaH was added. When no more gas was evolved, 5.99 g (30.7 mmol) **5** in THF was added. Stirring was continued at 0°C for one hour, then the solution was warmed to room temperature, washed with water and the aqueous phase was extracted with ether three times. The combined organic phases were dried over $MgSO_4$, filtered and the solvent removed under vacuum. Silica gel flash chromatography (50:1 petroleum ether:Et_2O) gave **6** as a yellow oil; yield 3.75 g (18.7 mmol, 61%) The spectroscopic data were in accordance with literature.[1] R_f (Petroleum Ether:Et_2O 50:1) = 0.17; ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm = 1.07 (t, *J*=7.51 Hz, 3 H), 2.14 - 2.28 (m, 2 H), 4.25 (d, *J*=6.60 Hz, 2 H), 4.43 (s, 2 H), 5.56 - 5.64 (m, 1 H), 5.68 - 5.76 (m, 1 H), 7.30 - 7.42 (m, 3 H), 7.47 - 7.56 (m, 2 H).

3-Benzylidene-4-propenyltetrahydrofuran (7). 10.0 mg (11.1 μmol) **8** and 2.0 mL 1,2-dichloroethane (freshly distilled under nitrogen, degassed) were added to a Schlenk tube.

H_2 was bubbled through the solution for 10 minutes followed by N_2 for another 10 minutes. 23 mg **6** (115 μmol) was injected into the stirring solution. The reaction was monitored by NMR and the reaction rates are discussed in the text. The spectroscopic data were in accordance with literature.[1] ^{1}H NMR (300 MHz, CD_2Cl_2) δ ppm 1.81 (dd, *J*=6.60, 1.47 Hz, 3 H), 3.42 - 3.55 (m, 2 H), 4.04 - 4.16 (m, 1 H), 4.61 (dt, *J*=14.29, 2.20 Hz, 1 H), 4.75 (d, *J*=14.29 Hz, 1 H), 5.41 (ddq, *J*=15.02, 7.69, 1.47, 1 H), 5.65 - 5.80 (dq, *J*=15.02, 6.36 Hz, 1 H), 6.28 - 6.34 (m, 1 H), 7.23 (s, 3 H), 7.34 - 7.44 (m, 2 H).

Gas Chromatography (GC): the determination of the enantiomeric excess (ee) was done with chiral GC by comparison with the racemic sample on an instrument described above (see Instrumentation). He carrier gas, 1.38 bar (20 psi); temperature program: initial temperature of 100°C, 0.4°C per minute up to 200°C. Retention times for the racemic sample of **7**: enantiomer 1: 122.58 minutes; enantiomer 2: 123.38 minutes. Starting material (**6**) had a retention time of 113.4 minutes.

[Rh((*R*)-BINAP)(NBD)]BF_4 (8). Under N_2, 41.3 mg (111 μmol) $[Rh(NBD)_2]BF_4$ and 5 mL freshly distilled and degassed CH_2Cl_2 were added to a Schlenk flask. While stirring, 68.9 mg (111 μmol) (*R*)-BINAP was added. Stirring continued for 2 hours. The solvent was removed and the solid washed with hexanes. ^{1}H NMR (400 MHz, CD_2Cl_2) δ ppm 1.65 (s, 1 H) 4.03 - 4.08 (m, 1 H) 4.76 - 4.83 (m, 1 H) 5.00 - 5.06 (m, 1 H) 6.50 (d, *J*=8.50 Hz, 1 H) 6.65 - 6.72 (m, 2 H) 6.77 - 6.84 (m, 1 H) 7.02 (ddd, *J*=8.21, 6.74, 1.17 Hz, 1 H) 7.34 - 7.40 (m, 3 H) 7.40 - 7.47 (m, 2 H) 7.52 - 7.58 (m, 3 H) 7.61 - 7.74 (m, 3 H); ^{13}C NMR (101 MHz, CD_2Cl_2) δ ppm 42.74, 48.09, 49.77, 125.65, 126.24, 126.33,

126.37, 126.92, 127.75, 127.87, 128.16, 128.35, 128.46, 128.84, 130.09, 130.33, 130.56, 133.28, 133.81, 134.03, 134.25, 135.11, 135.45, 137.40; ^{31}P NMR (162 MHz, CD_2Cl_2) δ ppm 28.48 (d, *J*=156.05 Hz); anal. calcd. for $C_{51}H_{40}BF_4P_2Rh$ (904.52): C 67.72, H 4.46; found C 67.02, H 4.57.

[Rh((*R,R*)-Norphos)(NBD)]BF_4 (9). Under N_2, 19.3 mg (67 μmol) $[Rh(NBD)_2]BF_4$ and 5 mL freshly distilled and degassed CH_2Cl_2 were added to a Schlenk flask. While stirring, 31.1 mg (67 μmol) (*R,R*)-Norphos was added. Stirring continued for 2 hours. The solvent was removed and the solid washed with hexanes and then recrystallized from CH_2Cl_2 and hexanes. ^{1}H NMR (400 MHz, CD_2Cl_2) δ ppm 0.81 (d, *J*=9.04 Hz, 1 H), 1.67 - 1.76 (m, 3 H) 2.51 (dd, *J*=16.98, 13.07 Hz, 1 H), 2.74 - 2.79 (m, 1 H), 3.02 - 3.10 (m, 2 H), 4.10 - 4.16 (m, 2 H), 4.74 - 4.81 (m, 2 H), 5.30 - 5.34 (m, 2 H), 5.35 - 5.40 (m, 1 H), 6.19 (dd, *J*=5.62, 3.18 Hz, 1 H), 7.24 - 7.34 (m, 4 H), 7.52 - 7.75 (m, 12 H), 7.75 - 7.82 (m, 2 H), 7.85 - 7.93 (m, 2 H); ^{13}C NMR (101 MHz, CD_2Cl_2) δ ppm 39.76 - 40.25 (m), 41.70 - 43.06 (m), 51.99, 55.94, 70.59, 81.97, 82.62, 89.87, 129.37 (d, *J*=10.72 Hz, 3 C) 129.76 - 130.08 (m), 130.81 (dd, *J*=9.28, 5.15 Hz) 131.33 (q, *J*=2.47 Hz) 131.48, 132.71 - 133.44 (m), 136.07 (dd, *J*=53.82, 12.58 Hz) 140.55 (d, *J*=7.42 Hz); ^{31}P NMR (162 MHz, CD_2Cl_2) δ ppm 27.95 (dd, *J*=157.03, 30.12 Hz, 1 P), 29.07 (dd, *J*=157.53, 30.12 Hz 1 P); anal. calcd. for $C_{38}H_{36}BF_4P_2Rh$ (744.35): C 61.32, H 4.87; found C 60.67, H 4.77.

[Rh((*R*)-5,5'-norimido-BINAP)(NBD)]BF_4 (10). Under N_2, 36.2 mg (96.8 μmol) $[Rh(NBD)_2]BF_4$ and 5 mL freshly distilled and degassed CH_2Cl_2 were added to a Schlenk flask. While stirring, 92.0 mg (96.8 μmol) (*R*)-5,5'-norimido-BINAP was added. Stirring

continued overnight. The solvent was removed and the solid washed with hexanes and was recovered in 92% yield. The ^{31}P NMR showed a 'doublet of doublets'. For further explanation of the ^{31}P NMR, see the text. ^{1}H NMR (400 MHz, CD_2Cl_2) δ ppm 1.68 (d, *J*=8.79 Hz, 2 H) 1.81 (d, *J*=8.79 Hz, 2 H) 1.93 (t, *J*=1.61 Hz, 2 H) 3.51 - 3.56 (m, 4 H) 3.56 - 3.66 (m, 4 H) 4.00 (br s, 2 H) 4.64 (br. s., 2 H) 4.95 (br. s., 2 H) 6.26 (dd, *J*=5.72, 2.78 Hz, 2 H) 6.36 (dd, *J*=5.64, 2.86 Hz, 2 H) 6.85 (d, *J*=8.06 Hz, 2 H) 6.99 - 7.07 (m, 12 H) 7.24 - 7.33 (m, 12 H) 7.46 (d, *J*=9.23 Hz, 2 H) 7.64 - 7.73 (m, 2 H); ^{13}C NMR (101 MHz, CD_2Cl_2) δ ppm 45.81, 45.99, 46.12, 46.30, 46.51, 47.25, 47.43, 50.66, 126.62, 126.69, 128.14, 128.51, 128.66, 128.72, 129.63, 129.99, 130.18, 130.54, 130.62, 131.33, 131.40, 131.91, 133.43, 134.35, 134.43, 134.48, 135.09, 135.18, 136.03, 136.20, 143.65, 176.75, 177.26; ^{31}P NMR (162 MHz, CD_2Cl_2) δ ppm 28.82 (br d, *J*=155.55 Hz), see text for analysis. anal. calcd. for $C_{69}H_{54}BF_4N_2O_4P_2Rh$ (1226.84) C 67.55, H 4.44, N2.28; found C 67.02, H 4.99, N 1.81.

[Rh((*R*)-BINAP)Cl]$_2$ (11). Under N_2, 27.3 mg (70.3 μmol) $[Rh(C_2H_4)_2Cl]_2$ and 5 mL freshly distilled and degassed CH_2Cl_2 were added to a Schlenk flask. While stirring, 87.6 mg (141 μmol) BINAP was added. Stirring was continued for 2 hours and nitrogen was blown over the solvent for brief intervals to remove evolved ethylene. The solvent was removed and the solid washed with hexanes. ^{1}H NMR (400 MHz, CD_2Cl_2) δ ppm 6.60 - 6.70 (m, 6 H) 6.74 (t, *J*=7.14 Hz, 2 H) 6.95 - 7.06 (m, 6 H) 7.12 (t, *J*=7.32 Hz, 2 H) 7.25 - 7.34 (m, 6 H) 7.44 (d, *J*=8.78 Hz, 2 H) 7.53 (d, *J*=7.87 Hz, 2 H) 7.78 - 7.85 (m, 4 H) 7.85 - 7.95 (m, 2 H); ^{13}C NMR (101 MHz, CD_2Cl_2) δ ppm 125.65, 126.24, 126.37, 126.92, 127.75, 127.87, 128.46, 128.84, 130.09, 130.33, 130.56, 133.28, 133.81, 134.03, 134.25,

135.10, 135.45, 137.40; ^{31}P NMR (162 MHz, CD_2Cl_2) δ ppm 50.01 (d, *J*=195.06 Hz, 2 P) anal. calcd. for $C_{88}H_{64}Cl_2P_4Rh_2$ (1522.06) C 69.44, H 4.24; found C 68.97, H 4.18.

[Rh((*R*)-5,5'-dinorimido-BINAP)Cl]$_2$ (12). Under N_2, 21.6 mg (55.5 μmol) $[Rh(C_2H_4)_2Cl]_2$ and 5 mL freshly distilled and degassed CH_2Cl_2 were added to a Schlenk flask. While stirring, 105.6 mg (111 μmol) (*R*)-5,5'-dinorimido-BINAP was added. Stirring continued for 2 hours, blowing nitrogen over the solvent for brief intervals to remove evolved ethylene. Attempted recrystallizations were unsuccessful. The solvent was removed and the solid washed with hexanes. The resulting ^{31}P NMR of the product gave several overlapping signals at 50.5 ppm. The P-Rh coupling was able to be determined out of the complex multiplets (198.8 Hz), resulting in a 'doublet of multiplets'. ^{1}H NMR (500 MHz, CD_2Cl_2) δ ppm 1.70 (d, *J*=9.28 Hz, 2 H), 1.83 (d, *J*=7.32 Hz, 2 H), 3.49 - 3.56 (m, 4 H), 3.56 - 3.71 (m, 4 H), 6.28 (dd, *J*=2.69 Hz, 2 H), 6.40 (dd, *J*=2.69 Hz, 2 H), 6.83 (d, *J*=7.08 Hz, 2 H), 6.95 - 7.11 (m, 14 H), 7.19 - 7.27 (m, 10 H), 7.35 - 7.44 (m, 2 H), 7.58 - 7.67 (m, 2 H); ^{13}C NMR (126 MHz, CD_2Cl_2) δ ppm 45.74, 45.78, 45.87, 45.88, 45.90, 46.06, 46.12, 46.17, 46.43, 46.46, 47.13, 47.14, 47.15, 47.34, 47.39, 47.41, 47.48, 52.67, 58.48, 60.25, 125.31, 125.56, 126.64, 127.22, 128.42, 128.51, 128.74, 129.32, 129.58, 129.82, 129.87, 134.02, 134.07, 134.11, 135.02, 135.07, 135.13, 135.20, 135.41, 135.48, 135.51, 135.78, 135.82, 135.89, 135.95, 136.03, 176.86, 176.99, 177.28, 177.32, 177.52; ^{31}P NMR (202 MHz, CD_2Cl_2) δ ppm 49.23 - 51.34 (dm, *J*=198.8 Hz); anal. calcd. for $C_{124}H_{92}N_4O_8P_4Rh_2$ (2166.69) C 68.74, H 4.28, N 2.59; found C 69.33, H 4.12, N 2.77.

General Procedure for Ring Opening Metathesis Polymerization and Deposition of Rh Catalysts. Under N_2, 10 mg of Rh catalyst was dissolved in freshly distilled and degassed CH_2Cl_2 in a presure flask. Freshly distilled cyclooctene (COE) was added to this mixture and allowed to stir for 5 minutes. Grubbs' catalyst, either first or second generation (see results and discussion for details), was added to the stirred mixture and the resulting solution was heated to 45°C until the polymerization was judged complete by ^{31}P NMR. A completed polymerization resulted in a broad peak in the NMR spectrum shifted downfield of where the sharp monomeric signals were present (see text for spectral examples).

Solid (1g) washed with CH_2Cl_2 was added to a Schlenk flask and placed under vacuum to dry for 1 h. The flask was backfilled with N_2 and, upon completion of the catalyst polymerization, the polymer solution was transferred into the Schlenk flask containing the washed and dried solid. The solvent was then slowly removed under vacuum while stirring the solid/solution mixture. The polymer catalyst was deposited on the solid support and was then washed with the reaction solvent 3 times before use in the cycloisomerization reaction.

General Procedure for [Ru(bisphosphine)C_8H_{11}]BF_4, [Ru(bisphosphine)(MeCN)(COD)]BF_4 and [Rh(NBD)(Bisphosphine)]BF_4 Catalyzed Cycloisomerization Reactions. Under N_2, 10 mg of Rh catalyst was added to a pressure flask in 2 mL freshly distilled and degassed solvent. In the case of polymerized catalyst use, the equivalent amount of supported catalyst was used to give 10 mg of catalyst. In both homogeneous

and heterogeneous cases, H_2 was bubbled through the mixture for 8 minutes followed by flushing with N_2 or Ar for 10 minutes. While stirring, the cycloisomerization substrate was added to the mixture and the reaction was monitored by ^1H NMR. The reaction rates are discussed in the text.

For reuse, in the case of the polymerized and deposited catalysts, the reaction was allowed to go for a set time. The stirring was then stopped and the supported catalyst was allowed to settle. The solution above the level of the solid was removed, with care taken not to allow the solid to go dry. The solid was then washed three times with the reaction solvent and removed in the same manner. After the third wash, the solvent was returned to the 2 mL level and, while stirring, the substrate was added once again. This procedure was repeated for subsequent runs.

General Procedure for [Rh(Bisphosphine)Cl]$_2$ Catalyzed Cycloisomerization Reactions. Under N_2, 10 mg of Rh catalyst was added to a pressure flask in 2 mL freshly distilled and degassed solvent. The cycloisomerization substrate was added to the mixture and allowed to stir for 5 minutes. 2.1 equivalents of $AgSbF_6$ (to catalyst) was then added to the mixture and reaction progress was monitored by ^1H NMR and the reaction rates are discussed in the text.

In the case of the polymerized and deposited catalysts, stirring was stopped and the supported catalyst was allowed to settle when the run was to be changed over. The solution above the level of the solid was removed, with care taken to allow the solid to

remain under solvent. The catalyst was then washed three times with the reaction solvent and removed in the same manner. After the third wash, the solvent was returned to the 2 mL level and, while stirring, the substrate was added once again. This procedure was repeated for subsequent runs.

General Procedure for Column Flow Reactors. A plug of glass wool and a layer of sand were placed in the bottom of a 0.5 cm diameter, 1 m long chromatography column and was flushed for 1 h with N_2. 1.25 g of 12.5 mg catalyst/g solid polymerized and deposited catalyst was placed on top of the sand followed by a second layer of sand. The entire column was then flushed with N_2 for 1 h. 15 mL degassed 1,2-dichloroethane was then passed through the column at a rate of 0.5 mL/min. The solvent layer was dropped to the top of the sand and a solution of $AgSbF_6$ and substrate was added to the column. The substrate solution was passed through at a rate of 2 mL/h. When the top of the solvent layer reached the sand layer, a second substrate solution, without the $AgSbF_6$ present, was added. This was repeated until a sufficient number of runs were completed.

1. Hashmi, A.S.K., P. Haufe, and A.R. Nass, *On the enantioselective rhodium-catalyzed enyne cyclization.* Advanced Synthesis & Catalysis, 2003. **345**(11): p. 1237-1241.